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THE CLINICAL SIGNIFICANCE OF GLYCOSURIA IN PREGNANT WOMEN.

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I know of no complication of pregnancy the significance of which is more variously interpreted than the presence of sugar in the urine of pregnant women. Certain writers regard it as a harmless almost physiological phenomenon, while others hold that it is always indicative of the existence of diabetes. Thus, Charrin, Brocard, Leduc, Salémi, and Bar state that a larger or smaller quantity of glucose can be demonstrated in the urine of from 40 to 66 per cent. of all pregnant women, and is, therefore, of no clinical significance. On the other hand Eshner, in 1907, collected the histories of 35 cases of diabetes complicating pregnancy, with a gross maternal mortality of 54 per cent. Moreover, it sometimes happens that the same case may be interpreted as a harmless and transient glycosuria, or as a mild case of diabetes, according to the point of view of the writer.

This divergence of opinion is in great part due to the influence exerted upon medical thought by a paper upon puerperal diabetes, which J. Matthews Duncan read before the London Obstetrical Society in 1882. At that time he collected from his own experience and the literature the histories of 22 pregnancies occurring in 16 women who had become pregnant while suffering from diabetes, or who had developed the disease during the course of pregnancy. Four died in coma or collapse within a few days after delivery and 7 others perished from diabetes or tuberculosis within the following two years, while 47 per cent. of the children were lost. He therefore

concluded that diabetes constituted one of the most serious complications of pregnancy, and his views were accepted without question, so that the practitioner, and even the obstetrical specialist, has come to regard the presence of sugar in the urine of pregnant women as of most serious prognostic import.

During the last five years I have seen a number of cases of glycosuria complicating pregnancy, and desire upon this occasion to call attention to my experience, and, after reviewing the literature upon the subject, to draw certain conclusions which I hope may be of practical value.

CASE I.—*Lactosuria in Pregnancy.* Mrs. H. J. B., aged thirty years, pregnant for the fourth time. Definite reduction with Fehling's solution occurred in the seventh lunar month, continued at intervals until the birth of the child, and disappeared entirely after the tenth day of the puerperium. The sugar varied between 1 and 2 per cent. in amount and did not undergo fermentation. At no time were any untoward symptoms noticed. An 8½-pound child was born after an operative labor; the puerperium was normal. Sugar did not reappear in the course of the following two years.

CASE II.—*Transient Glycosuria in Pregnancy.* Mrs. J. M. K., aged twenty-five years, pregnant for the first time. Three months before labor sugar appeared in the urine, and was demonstrated repeatedly during a period of three weeks, after which it disappeared spontaneously and did not return. It varied from 0.5 to 1 per cent. in amount, and readily underwent fermentation. There were no symptoms and the daily output of urine varied between 1200 and 1800 c.c. An 8½-pound child was delivered after an easy low-forceps operation; the puerperium was normal. Sugar did not reappear in a subsequent pregnancy three years later.

CASE III.—*Transient Glycosuria in Pregnancy.* Mrs. G. D. P., aged forty-three years, a stout woman, pregnant for the sixth time. Specimens of urine examined during the fourth and fifth months were normal. About the middle of the sixth month she began to complain of considerable thirst, and stated that her appetite was abnormally large as compared with that noted in previous pregnancies. The urinary output varied between 1500 and 2000 c.c. and contained from 1.3 to 2 per cent. of glucose on ordinary diet. Upon placing her upon an antidiabetic diet the sugar did not entirely disappear, but decreased to about 0.125 per cent., becoming abundant whenever a more liberal diet was permitted. The symptoms gradually subsided, although traces of glucose could be detected up to the time of labor, but disappeared permanently during the puerperium, being entirely absent from a specimen examined on the tenth day. The labor and puerperium were normal and the child weighed 8¾ pounds.

CASE IV.—*Alimentary Glycosuria in Pregnancy.* Mrs. D. K. B. (*a*) The patient when first seen was twenty-four years of age and in

her second pregnancy. Two months before labor the presence of sugar was demonstrated upon repeated occasions, and, after persisting for six weeks, passed off spontaneously. There were no symptoms, and the daily output of urine varied from 1500 to 2000 c.c. The sugar varied between 0.25 and 1 per cent. in amount, and consisted of a mixture of glucose and lactose; as positive results were obtained both by the polariscope and by fermentation, the former indicating a much larger quantity of sugar than the latter. After a spontaneous labor she gave birth to a live child weighing 8¼ pounds, and had no further trouble until the next pregnancy. (*b*) Three years later she became pregnant for the third time and sugar made its appearance during the seventh lunar month, persisting in varying quantities up to the birth of the child. She presented no symptoms and passed in twenty-four hours from 2000 to 2500 c.c. of urine, which contained from 0.25 to 1 per cent. of glucose. Its quantity remained unchanged no matter whether she was upon an ordinary or a carbohydrate-free diet. On discussing the matter with the patient I found that she had suffered from comstipation for years and used senna prunes for its relief. These were prepared by stewing one pound of prunes in a decoction of a handful of senna leaves in a quart of water, to which one pound of sugar was added, which was then evaporated down to a thick syrup. Each night she took one-half dozen or more of prunes with considerable quantity of the syrup. It occurred to me that the glycosuria might possibly be due to the fact that she was unable to assimilate this extra amount of sugar. This supposition was found to be correct, as all trace of sugar disappeared from the urine upon replacing the prunes by a simple purgative, but it would promptly reappear as soon as their use was resumed. In this instance it appeared that the patient was intolerant of sugar administered in this form and suffered from alimentary glycosuria whenever it was used, but at the same time was able to assimilate the carbohydrates in her ordinary diet. She gave birth to an 8¼-pound child after a normal labor, and no trace of sugar could be found after the puerperium.

Case V.—*Recurrent Glycosuria during Pregnancy.* Mrs. J. T H. (*a*) She became pregnant for the first time when twenty-nine years of age. The pregnancy was perfectly normal up to the seventh month when glycosuria appeared and continued until the time of labor, but gave rise to no symptoms. The amount of glucose varied from a mere trace to 0.5 per cent. and was uninfluenced by diet. A well-developed child was born after a normal labor and no trace of sugar could be detected during lactation. (*b*) The second pregnancy began eleven months after the birth of the first child. Sugar was detected at the second month and persisted in varying quantities until the time of labor. It varied from a mere trace to 1 per cent. and was definitely shown to be glucose. The glycosuria was not influenced by diet and gave rise to no symptoms. Pregnancy and

labor were uneventful and the sugar disappeared immediately after the latter. (*c*) Her third pregnancy occurred four years after the birth of the second child. Repeated examination showed that the urine was free from sugar up to the sixth month, at which period it made its appearance and persisted up to the time of delivery. Chemical examination showed that it was definitely glucose, and ordinarily varied between 0.25 and 0.5 per cent. The glycosuria was not influenced by carhohydrate-free diet, and gave rise to no symptoms; acetone bodies were at no time present. The patient passed through a normal pregnancy, labor, and puerperium, and no trace of sugar could be found later.

CASE VI.—*Mild Diabetes complicating Pregnancy.* Mrs. L. W., aged twenty-nine years, came to the hospital in the seventh month of her second pregnancy, her physician having discovered the existence of glycosuria a few weeks previously. She complained of frequent micturition and stated that she was obliged to drink large quantities of water on account of excessive thirst, but had observed no other symptoms. On the day of admission she passed 1000 c.c. of urine which contained 2.5 per cent. of glucose. The glycosuria disappeared entirely upon a milk diet, but reappeared when she was placed upon a restricted ward diet, the urine containing 0.46 to 0.50 grams of glucose per liter. After remaining in the hospital for two weeks she was dismissed in good condition with instructions as to diet. Her physician has kindly informed me that she remained in good condition during the rest of her pregnancy upon a restricted diet, and had a normal labor at term. Six months later her urine contained 3 per cent. of glucose with a specific gravity of 1044. She presented no symptoms and would have been unaware of her condition were it not for the fact that she was kept under constant supervision and upon a restricted diet.]

The histories which I have briefly given serve as examples of the various conditions in which sugar may be observed in the urine of pregnant women. Thus in Case I we had to deal with simple lactosuria, in Cases II and III with transient glycosuria, in Case IV with alimentary glycosuria, in Case V with recurrent glycosuria, and in Case VI with mild diabetes. With the exception of the latter, all of the cases were observed in private practice.

By way of comparison I have gone over the urinary records of 0300 consecutive patients in the Obstetrical Department of the Johns Hopkins Hospital. In this series the urine was examined as a matter of routine by the assistant or student on duty at weekly intervals, except for a catheterized specimen obtained immediatey after labor, and the presence of sugar was recorded only when a definite reduction was obtained with Fehling's solution. Judged by this criterion, sugar was demonstrated in 167 patients during pregnancy, labor, or the purperium, a frequency of 5.57 per cent.

The incidence in the several periods was as follows: Pregnancy alone, 24 cases (0.8 per cent.); puerperium alone, 137 cases (4.57 per cent.); and in both pregnancy and puerperium, 6 cases (0.2 per cent.).

Upon analyzing the cases in which the presence of sugar was demonstrated only during pregnancy, it is found that it was noted in 12 instances two weeks before labor, in 6 instances between two and four weeks before labor, in 4 instances between four and eight weeks before labor, and in 2 instances during the sixth and seventh months of pregnancy, respectively. The last 2 cases were examples of definite glycosuria, one being the case of diabetes whose history was given above (Case VI); while unfortunately no particulars can be given concerning the other, as she insisted upon leaving the hospital after a stay of only a few days, and has not been heard from since. It may be assumed that the majority of the other 22 cases were examples of lactosuria, as in no instance in which the nature of the sugar was determined was if found to be glucose. Moreover, its appearance so late in pregnancy would indicate that it was associated with premature mammary activity. Likewise, in all probability, we had to deal with lactosuria in the six cases in which a reduction was obtained both in pregnancy and the puerperium, as in each instance sugar appeared only shortly before labor, but unfortunately its exact nature was not determined.

In all of the 137 cases in which the presence of sugar was demonstrated only during the puerperium, we presumably had to deal with lactose. This belief is based upon the fact that the condition was usually associated with abnormalities in the mammary secretion, and furthermore that fermentation failed to occur in any of the cases subjected to that test, although of course it is possible that occasionally it may have been combined with glucose; but positive statements cannot be made in this regard, as in no instance were the characteristic osazones isolated.

Naturally, the 167 cases here mentioned do not represent the actual incidence of the presence of sugar in the urine during the last weeks of pregnancy and the first two weeks of the puerperium, for the reason that the examinations were made only once a week and a positive result recorded only when a definite reduction was obtained with Fehling's solution. Doubtless, a much greater incidence would have been indicated had daily examinations been made with more delicate reagents.

I shall now turn to the literature upon the subject and shall consider separately each of the following conditions: (*a*) Lactosuria; (*b*) transient glycosuria; (*c*) alimentary glycosuria; (*d*) recurrent glycosuria; and (*e*) diabetes.

Lactosuria. Although the presence of sugar in the urine of puerperal women was mentioned by Heller in 1849, it was first brought prominently to the attention of the profession in 1856, by Blot, who

stated that he had been able to demonstrate it in amounts varying between 1 and 2 grams per liter in 45 consecutive women who suckled their children. He held that its presence was dependent upon the functioning of the breasts and that its quantity served as an idex of the abundance of the milk supply. Moreover, he stated that sugar could be found in the urine of about 50 per cent. of women in the last weeks of pregnancy. Unfortunately, he designated the condition as "physiological glycosuria," but did not attempt to determine whether the sugar in question was glucose or lactose. This communication aroused great interest and gave rise to a discussion which has extended to the present time.

Blot's statements were promptly tested by a number of investigators, some of whom absolutely denied their correctness and attributed his results to faulty technique, while others confirmed them more or less fully. Thus, Wiederhold, Leconte, Capezzuoli, Riedel, Iwanoff, and others stated that sugar was not present under such circumstances and that the reduction of the copper solution, which had been attributed to it, was due to the presence in the urine of mucus, uric acid, creatinin, or other substances. On the other hand, De Moulins, Kirsten, Brücke, Lecoq, Chailly, Louvet, Hempel, De Sinéty, Gubler, and Johannovsky demonstrated the presence of sugar in the urine of a varying proportion of puerperal women.

It is interesting to note that De Moulins, Wiederhold, Lecoq, and others suggested that the sugar in question might be lactose, while De Sinéty demonstrated that it disappeared in animals upon amputating the breasts and failed to appear after subsequent labors. Moreover, all investigators who obtained positive results were united in stating that the largest quantities of sugar were noted in women who did not suckle their children or in whom the breasts had become engorged from one cause or another, and accordingly attributed it to resorption. Consequently they concluded that Blot's contention was erroneous concerning the value of the condition as an index of mammary activity.

In 1877 and 1879 Hofmeister and Kaltenbach, respectively, isolated the sugar in question and definitely showed that it was lactose, thereby conclusively demonstrating that the condition was one of lactosuria, and that the term glycosuria was a misnomer. They held that the condition in all probability was due to the resorption of lactose from the milk in the more or less engorged breasts, and was, therefore, associated with their imperfect functioning. The suggestion of Luther that milk sugar, which thus gained access to the blood current, did not pass through the portal system, as well as the demonstration by Moritz and Voit that it was excreted unchanged through the kidneys when injected directly into the circulation, whereas it was utilized for metabolic purposes when administered by the mouth, afforded a thoroughly satisfactory explanation for the production of the phenomenon.

Notwithstanding the demonstration of the nature of the sugar in these cases, the majority of subsequent writers failed to make use of the term "puerperal lactosuria," but continued to designate the condition as glycosuria, puerperal diabetes, or resorption diabetes, as the case might be, and thereby materially retarded the general recognition of its true significance. Following the establishment of the mode of production of puerperal lactosuria, all investigators, who have made daily examinations of the catheterized urine of puerperal women, have been able in most cases to demonstrate the presence of traces of lactose at some time during the first few days of the puerperium, as well as considerable quantities whenever the breasts became engorged or the child was weaned. Observations of this character have been made by McDonald, Davenport, Ney, McCann and Turner, Lemaire, Keim, Leduc, Queirel and Domergue, Commandeur and Porcher, and others.

In view of these findings, the existence of slight degrees of lactosuria (0.5 to 1 gram per liter) in the early days of the puerperium may be regarded as perfectly physiological, while the presence of larger quantities (10 to 30 grams per liter) may be expected whenever the breasts become engorged or the child is weaned. The fact that sugar was found in only 143 out of 3000 puerperal urines in my service should not be regarded as invalidating this statement, for two reasons: In the first place, as our urines were examined only once a week, such a transient phenomenon occurring between the second and fourth days would frequently escape detection; and, secondly, as the examinations merely formed a part of the routine duties of the assistant on duty, it is highly probable that only such cases would be reported which presented a perfectly typical reduction with Fehling's solution, which is not observed unless at least 1 per cent. of sugar is present.

In this connection it is important to direct attention to the diagnostic significance of lactosuria accompanying the process of weaning the child, as in such cases the quantity of sugar may rise as high as 3 or 4 per cent. and persist until the secretion has been checked and the breasts have become soft and flabby. For this reason, the detection of sugar in the urine of a nursing woman who has just weaned her child in order to enter a hospital, for example, should not lead to the diagnosis of diabetes until the nature of the sugar has been definitely determined: as it may readily happen that failure in this regard may lead to the postponement of a necessary operation or to erroneous conclusions concerning the prognostic significance of diabetes complicating surgical procedures. Attention was first directed to this fact by Sir W. J. Sinclair as early as 1886.

Lactosuria of Pregnancy. The observations of Bar, Brocard, Bürgers, Commandeur and Porcher, Ludwig, Naunyn, and others have clearly shown that by appropriate means slight degrees of lactosuria may also be detected during the last weeks of pregnancy

and is usually associated with premature mammary activity. Thus, Ludwig noted it in 46 per cent. of 82 women in the last weeks of pregnancy, while in 10 per cent. more of his patients lactose alternated with glucose. Commandeur and Porcher found lactosuria in 30 consecutive cases, although in 8 instances it was associated with glycosuria. In the latter event they believe that the condition is due to the fact that the breasts are not sufficiently active to convert into lactose all of the glucose which is brought to them by the blood, as they hold that such a transformation usually occurs as soon as the breasts begin to function. Moreover, they consider that both they and Bert have adduced experimental evidence in support of such a transformation by finding that the urine of recently delivered goats, whose breasts had been amputated just before conception, contains considerable quantities of glucose in place of the lactose which is usually present.

In 22 of the 24 cases in which sugar was present during pregnancy in the urine of 3000 consecutive patients in my service, it is probable that we had to do with lactosuria, as in none of them was the presence of sugar demonstrated prior to the last six weeks of pregnancy and usually only during the two weeks immediately preceding delivery. Moreover, only lactose was found in the cases in which the nature of the sugar was differentiated. On the other hand, Case I clearly shows that lactosuria does not occur exclusively in the last weeks of pregnancy, as in this instance milk sugar was definitely demonstrated during the course of the seventh month, and doubtless many similar cases have occurred in the experience of others.

In consideration of the facts just adduced, I feel that one is justified in stating that moderate degrees of lactosuria occurring either during pregnancy or the puerperium may be regarded as physiological and, therefore, of no prognostic significance. The practical importance of the condition lies in the fact that an incautious observer may confound it with glycosuria and, believing that the latter is indicative of the existence of diabetes, may express a sombre prognosis, which is usually not justifiable.

Transient Glycosuria. Leaving out of consideration the minute amounts of glucose which have been shown by the observations of Brücke, Ivanoff, Abeles, Pavy, Luther, Moritz, Lemaire, and others to be present in the urine of normal men and women, certain authors also state that appreciable quantities of glucose may be demonstrated in the urine during the second half of pregnancy and particularly during its last few weeks. The following authors make varying statements concerning its incidence: Keim, 10 per cent.; Ludwig, 12 per cent.; Ney, 16.6 per cent.; Commandeur and Porcher, 26 per cent.; Charrin, 40 per cent.; Bar, 43 per cent.; Brocard, 45 per cent.; Leduc, 60 per cent.; Salémi, 66 per cent; while Rudaux holds that its presence is practically universal, and Brocard and Bar state

that glycosuria is observed much more frequently in multiparous than primiparous women.

Manifestly, in such cases the amount of glucose is very small, varying from 1 to 2 or 3 grams per liter, and consequently must be tested for by delicate reagents, as the presence of at least 1 per cent. is necessary in order to give a characteristic reduction with Fehling's solution. On the other hand, it not infrequently happens that larger quantities may be observed during pregnancy and yet have no connection with diabetes. This is clearly demonstrated by the histories of Cases II and III, as well as by many other instances which might be adduced from the literature. Exceptionally, the amount of sugar may rise as high as 3 or 4 per cent., and even give rise to slight symptoms, such as pruritus, increased thrist, and frequent urination, although subjective manifestations are usually absent. In either event, the glycosuria may disappear spontaneously after a longer or shorter period, or may persist throughout the balance of the pregnancy to disappear definitely after the birth of the child. It would appear that many physicians, being ignorant of the possibility of such an occurrence, have described cases of this character as examples of true diabetes, and it would seem that the cases described as such by Partridge, Taylor, Durieux, and others might be placed in this category.

Unfortunately, it is frequently impossible in a given case to determine immediately whether the presence of sugar is merely an evidence of transient glycosuria or of mild diabetes, and in many instances an assured diagnosis can be made only after the conclusion of pregnancy. If the condition is merely transient glycosuria, all traces of sugar promptly disappear after delivery and there are no further symptoms; whereas in diabetes the glycosuria persists and in many instances the symptoms become aggravated. The importance of recognizing the existence of transient glycosuria and of not confusing it with diabetes has been strongly insisted upon by Naunyn, Senator and Kamminer, Salus, Brook, and others. Very exceptionally the condition may still further similate diabetes, particularly as it is sometimes associated with hydramnios, as in the cases reported by Rossa in which the maternal urine contained 0.92 per cent. of glucose, while 0.345 per cent. was present in the amniotic fluid.

On inquiring as to the significance of transient glycosuria, it may be said that the milder degrees (1 to 2 grams per liter) should be regarded as practically physiological, while, on the other hand, the occurrence of larger quantities must be considered abnormal, although as far as our knowledge at present goes, not necessarily of clinical significance.

The most important practical point in connection with this condition, however, is to realize that it does occur, and that it is even quite common. Therefore, when the presence of glucose is demonstrated in the urine of pregnant women, diabetes should not be

diagnosticated, unless the sugar is present in large amounts and is accompanied by definite symptoms. Unfortunately, as has already been indicated, it is frequently impossible to differentiate between the two conditions until after delivery, as was clearly demonstrated in Cases III and IV. In both instances 2 per cent. of glucose was observed during the course of pregnancy and gave rise to no symptoms. In Case III the sugar disappeared immediately after delivery, while in Case IV it did not, but actually increased in amount, thus indicating that the former was an example of transient glycosuria and the latter of mild diabetes. The mode of production of this variety of glycosuria will be taken up under the following heading:

Alimentary Glycosuria. In 1895 Lanz and von Jaksch pointed out that women were less tolerant of sugar during pregnancy than at other times, and that transient glycosuria frequently followed the ingestion of an amount of glucose which would have been thoroughly assimilated by a non-pregnant woman. Investigations upon similar lines have since been undertaken by Keim, Brocard, Payer, Ludwig, Combemale and Oui, Charrin and Guillemonat, Schroeder, Rudaux and Bar, all of whom, with the exception of Ludwig, have more or less fully confirmed the findings of Lanz and von Jaksch. Thus Brocard administered to 17 pregnant women varying quantities of glucose before breakfast, and was able to demonstrate its presence in the urine in a varying proportion of cases within the course of the following two hours. He also found that alimentary glycosuria sometimes occurred in non-pregnant women, but far less frequently. The following table gives an idea of the varying effect of increasing doses of sugar in the two conditions:

	Per cent. of pregnant women.	Per cent. of non-pregnant women.
50 grams caused glycosuria in	50	11
80 grams caused glycosuria in	70	15
100 grams caused glycosuria in	70	16
150 grams caused glycosuria in	88	19
200 grams caused glycosuria in	100	29

Payer likewise experimented upon 45 pregnant women, 35 of whom manifested alimentary glycosuria, the average amount of glucose necessary to give rise to the phenomenon being 130 grams in pregnant, as compared to 200 grams in non-pregnant women. Schroeder, in 1905, performed similar experiments with levulose, and after a dose of 150 grams administered before breakfast obtained positive results in 17 out of 95 women. Moreover, it is important to note that all but 2 of his positive cases presented moderate degrees of albuminuria, which was of a very high grade whenever the levulosuria was marked. Combemale and Oui, and Bar have also observed more or less similar results following the administration of

cane sugar. Bar, who conducted a most careful series of experiments, calculated the amount which could be assimilated for each kilogram of the patient's weight, and found that the power of assimilation was greatly reduced during pregnancy; his experiments showed that glycosuria would follow the administration of 6 to 8 grams of sugar per kilo of body weight in pregnant as compared to 12 or 13 grams in non-pregnant individuals.

There is no doubt that alimentary glycosuria occurs comparatively frequently in practice and has occasionally been described as diabetes. Case IV was a striking example of this condition, and in it the glycosuria could be made to appear or disappear according as senna prunes were used as a laxative or not.

Numerous theories have been advanced in explanation of this phenomenon, and, while none of them are entirely satisfactory, we are obliged to reckon with the fact that the pregnant woman is less tolerant of sugar than at other times, and that, therefore, the practitioner will occasionally have to deal with cases of alimentary glycosuria. Moreover, it is quite possible that the same factors which are concerned in its production apply equally well to transient glycosuria.

Keim and others have advanced the theory that glycosuria in pregnancy is merely a manifestation of a toxemia. They hold that the latter is associated with disturbed function of the liver, by which the conversion of glucose into glycogen may be interferred with, thus leading to the production of glycemia and consequent glycosuria. Schroeder takes a somewhat similar view, which is based upon the fact that albuminuria was present in 15 out of 17 cases in which he was able to produce alimentary levulosuria. As he believes that the albuminuria of pregnancy is associated with abnormalities in the function of the thyroid gland, he is inclined to attribute the lessened power of assimilation of sugar to some similar derangement, although his view has not been accepted by most writers upon the subject. Brocard, on the other hand, holds that glycosuria is merely an expression of a diminished necessity for the consumption of carbohydrates during pregnancy, while Bar contends that it is a manifestation of a diminished power of assimilation. It is apparent, however, that these explanations are of but little value, as they throw no light upon the ultimate factors underlying the disturbed metabolism.

Rudaux, and Commandeur and Porcher associated the production of glycosuria with the mammary function. Rudaux believes that large quantities of glycogen are stored up in the liver and other organs in anticipation of lactation. Consequently, when this has been accomplished beyond a certain extent it becomes impossible for the usual amounts of glucose to be transformed into glycogen and thus be removed from the circulation, so that it becomes necessary for the excess to be excreted through the kidneys. Commandeur and Porcher, on the other hand, attribute the condition to lack of function

on the part of the breasts; they believe that during lactation the latter convert into lactose large quantities of glucose brought to them by the blood, and that normally this function becomes inaugurated in the last weeks of pregnancy. In connection with these theories, the observations of Charrin and Guillemonat are of interest, as they have apparently definitely shown that the liver cells of pregnant guinea-pigs contain far more glycogen than usual. They attribute this to lessened consumption, and hold that the overloaded cells are unable to take up the usual quantity of glucose from the blood and consequently glycemia and subsequent glycosuria must result.

Hofbauer, in his important recent contribution to our knowledge of the toxemias of pregnancy, studied the livers of several perfectly normal pregnant women who died from traumatism, and in each instance discovered characteristic changes in the liver cells, which he believes are normally associated with pregnancy. These consist in more or less fatty degeneration of the peripheral portions of the lobules, associated with a marked diminution in the glycogen content. If his observations hold good, it would appear that the cause of glycosuria must be sought in some abnormal condition of the liver cells resulting from pregnancy which interferes with the storage of glycogen in the ordinary quantities, so that the portion of sugar which should be so transformed must of necessity circulate in the blood and be excreted through the urine. It is interesting to note that Cristalli advanced a somewhat similar explanation in 1900.

Notwithstanding the large amount of work which has been done upon the subject, it is apparent that we are as yet unable to give a satisfactory explanation for the production of either transient or alimentary glycosuria, but at the same time it must be admitted that their occurrence is a fact which must be reckoned with and is of great diagnostic importance. In the present stage of our knowledge it would seem permissable to diagnosticate alimentary glycosuria in any case in which the sugar disappeared from the urine upon removing excessive quantities of sugar from the diet, while not restricting other forms of carbohydrate food.

Recurrent Glycosuria. Case V is a typical example of this condition. The patient presented glycosuria in three consecutive pregnancies, which varied in amount from a fraction of 1 to 2 per cent.; it gave rise to no symptoms, was not influenced by diet, disappeared after labor, and reappeared in each subsequent pregnancy.

It is interesting to note that two of the earliest cases described as diabetes in pregnant women were presumably of the same character, namely, those reported by Bennewitz and Lever in 1826 and 1847, respectively. Matthews Duncan was acquainted with the condition and drew from it the conclusion that "diabetes may occur only during pregnancy, being absent at other times." Likewise, Partridge, in 1895, in describing what he considered to be a case of diabetes complicating pregnancy, but which was probably only

an example of transient glycosuria, stated among other conclusions, that "diabetes may originate during pregnancy, persist throughout its course, and disappear on its completion to reappear in a subsequent pregnancy." Somewhat similar cases have been reported by Ruoff and Tate. In the former case 4 to 7 per cent. of sugar was present in the second, fourth, and fifth pregnancies, but disappeared during the puerperium in each instance. In Tate's case sugar was present in the second and third pregnancies and disappeared after the birth of the child.

It is difficult to speak positively concerning the significance of such cases. In those described by Bennewitz and Ruoff, the patients presented definite diabetic symptoms during pregnancy, and excreted large amounts of sugar, but the fact that the condition cleared up immediately after delivery and gave no further trouble until the occurrence of a subsequent pregnancy, would strongly militate against its diabetic nature. On the other hand, in the case reported by Tate, as well as in my Case VI, there were no symptoms and the condition was discovered simply on account of the routine examination of the urine. Whatever may be thought of the first group of cases, it seems clear that the latter group cannot be classified as diabetes, and is best described as recurrent glycosuria. At the same time it is probable that they should be regarded as of a more serious nature than ordinary transient or alimentary glycosuria, in that they probably indicate the existence of a more profound and continuous disturbance of metabolism.

Diabetes. Our knowledge upon this subject practically began with Duncan's paper in 1882, which was based upon the study of 22 pregnancies occurring in 16 women. Four of these died in coma or collapse at the time of labor, and 7 others perished from diabetes or tuberculosis in the course of the following two years, while 47 per cent. of the children were either born dead, succumbed during labor, or died early in the puerperium. As the result of his investigations he held that the association of pregnancy and diabetes was a most serious complication and formulated the following conclusions: (1) "Diabetes may come on during pregnancy." (2) "Diabetes may occur only during pregnancy, being absent at other times." (3) "Diabetes may cease with the termination of pregnancy, recurring some time afterward." (4) "Diabetes may come on soon after parturition." (5) "Diabetes may not return in a pregnancy occurring after its cure." (6) "Pregnancy may occur during diabetes." (7) "Pregnancy and parturition may be apparently unaffected in its healthy progress by diabetes." (8) "Pregnancy is very likely to be interrupted in its course and probably always by the death of the fœtus."

Considering these conclusions in the light of our present knowledge, it would appear that the conditions described under conclusions 2 and 5 probably possessed no points in common with diabetes,

except the presence of sugar in the urine, and were merely examples of transient, alimentary, or recurrent glycosuria. Moreover, as will be shown farther on, Duncan apparently took a somewhat too serious view of the dangers of true diabetes when associated with pregnancy.

Such a point of view can be readily understood, when it is remembered that at the time at which he wrote very few physicians were in the habit of examining the urine of apparently normal pregnant women at frequent and regular intervals, and made such examinations only in the presence of more or less serious symptoms. Consequently the majority of the cases of simple glycosuria must have escaped detection, and practically only the more serious forms of true diabetes were diagnosticated. That this interpretation is justifiable is shown by the fact that none of the six cases reported in this article would have been recognized had the frequent examination of the urine not formed part of the routine care of all pregnant women. On the other hand, as has already been indicated, Duncan's series of cases included several examples of non-diabetic glycosuria, which were probably more or less accidently discovered and described as diabetes in the absence of more precise information. Indeed it may be said that all statistics upon the subject have suffered from this defect, as the authors in their anxiety to collect a large series of cases have included a number of questionable significance.

From my own experience and a study of the literature I feel that the significance of diabetes associated with pregnancy may be profitably discussed under following headings: (*a*) Pregnancy may occur in definitely diabetic women. (*b*) Diabetes may be first recognized during pregnancy and persist afterward. (*c*) Diabetes may first appear during pregnancy and disappear afterward. (*d*) Diabetes may recur in each pregnancy and disappear after each delivery. (*e*) Diabetes may exist before and after pregnancy, but disappear during its course.

There can be no doubt as to the significance of the conditions described under the headings *a* and *b*, as in them the existence of diabetes can be readily established. The same may be said of group *e*, although the case described by Stengel is at present the only one belonging in the category. On the other hand, the diabetic nature of the conditions included in groups *c* and *d* is open to discussion, as they probably merely represent exaggerated examples of transient, recurrent, or alimentary glycosuria. Skepticism in this regard is justified by our conception of diabetes as a chronic, practically incurable disease, in which glucose is never long absent from the urine; therefore it would not appear permissible to describe as such, conditions in which the sugar permanently disappears.

One of the great merits of Duncan's work was that it clearly proved that pregnancy might occur in women suffering from diabetes, and thus did away with the old view that they were absolutely sterile.

At the same time it is generally admitted that the probability of conception becomes markedly diminished in such cases, partly because the disease usually occurs after the menopause, but more especially as the researches of Loeb, Hofmeier, Nebel, Seegen, Lecorché, and others have shown that it may be associated with profound changes in the internal genitalia. These may vary from a simple endometritis to marked atrophic processes in the ovaries or in the uterus, by which the ova are destroyed in situ or the uterus rendered unfit for their proper implantation and nutrition.

It is probably in great part due to partial persistence of the older view that most writers state that diabetes occurs much more frequently as a complication of pregnancy than that conception takes place in diabetic women. Thus Eshner, in 1907, stated that the latter occurred in only 8 out of 33 cases. On the other hand, I am inclined to hold that such a belief is erroneous and is based upon incorrect interpretation. The mere fact that the presence of sugar was first detected during the course of pregnancy by no means proves that it had not been present previously, but merely indicates that the condition was not accompanied by symptoms sufficiently severe to make it necessary for the patient to consult a physician. In such cases a diagnosis would not have been made had not the occurrence of pregnancy lead to the examination of the urine, just as it frequently happens that the existence of diabetes is unexpectedly discovered in men applying for life insurance, who had previously believed that they were in perfect health.

The accompanying table, which is based upon the histories of 66 definite cases of diabetes in pregnant women which I have collected from the literature, shows that in 55 instances the disease was present before the occurrence of the pregnancy in question, while in the remaining 9 it made its first appearance after conception. In this series no case was classified as diabetes unless the characteristic urinary changes persisted after the puerperium, for had the ordinary cases of glycosuria been included it is quite probable that the relationship would have been reversed. At the same time I do not desire to claim that my figures are beyond peradventure, but they at least clearly indicate that diabetes may exist anterior to conception in a much larger proportion of cases than is generally believed.

Upon reviewing the literature upon the subject, it is apparent that diabetes must be regarded as a serious condition no matter whether occurring primarily or as a complication of pregnancy, as is shown by the following figures: Thus, Chapiet, Stengel, Ruoff, and Vinay reported a maternal mortality of 25, 26, 46, and 55 per cent., respectively, in four tabulations which included 68, 19, 28, and 34 cases. My own statistics, which are based upon 66 cases collected from the literature, show an immediate maternal mortality of 27 per cent., while an additional 23 per cent. of the patients died within the following two years.

Generally speaking the patients do comparatively well for the first seven or eight months of pregnancy, although they may suffer considerably from pruritus, increased thirst, ravenous appetite, and frequent micturition. Exceptionally coma may supervene in the latter part of pregnancy, and the patient may die undelivered or shortly after the birth of the child, as reported by Born, Hofmeier, and others; although occasionally, as in the case reported by Offergeld, she may rally from the comatose condition and die weeks or months later. More usually, however, symptoms do not appear until the time of labor, and in such cases the patient may die either in coma or collapse within a few hours after the birth of the child; but even at this time coma is not necessarily fatal, as recovery has been reported and the patients have lived for some time afterward.

On the other hand, in a considerable proportion of cases, labor and the puerperium go on normally, while the diabetes pursues its usual course and leads to death in coma or from tuberculosis months or even years later. Moreover, it is a well-established fact that certain subjects may repeatedly give birth to children with comparative impunity. This occurred in Case VI, and was strikingly exemplified by the experience of Lecorché and Lop. The former reported that uncomplicated pregnancy and labor had occurred in seven of his patients, while the latter stated that four women under his care had gone through 6, 3, 2, and 1 normal labors respectively, after the diagnosis of diabetes had been definitely established.

I have included among the diabetic cases only such patients as died with characteristic symptoms, or in whose urine the presence of glucose was repeatedly demonstrated after childbirth. If this precaution be not taken many cases, which are merely examples of some of the other forms of glycosuria, will be improperly placed in this category. In order to illustrate this point I have included in Section "C" of my table 10 cases which are usually described as diabetic by other writers, but from whose urine all trace of sugar disappeared immediately after delivery. These ten women had twelve children with no maternal mortality and but two fœtal deaths, a result which is so striking as to cast grave doubt upon the correctness of the diagnosis.

The deleterious effects of diabetes whether existing before conception or appearing during the course of pregnancy are not limited to the mother, as a review of the literature shows that the child suffers equally severely. Thus abortion and premature labor occur more frequently than usual, and even if the pregnancy goes on to term it is not unusual for the child to die shortly before the onset of labor and to be born in a more or less macerated condition. Moreover it seems that the condition frequently predisposes to excessive development on the part of the child, which may give rise to serious dystocia and lead to its death during delivery.

Some idea of the increased danger to the child may be gained from

the tabulations of Chapiet, Duncan, Vinay, Stengel, and Ruoff, according to which the fœtal mortality was 27, 47, 48, 50, and 53 per cent. respectively. Chapiet's figures are based upon the largest series of cases: 103 pregnancies occurring in 68 women.

One of the interesting complications associated with the condition is hydramnios, with its serious effect upon the development of the child and its tendency toward the production of premature labor. I have been able to collect from the literature twelve examples of this condition, namely, the cases reported by Duncan, Reid, Husband, Warner, Hehir, Ludwig, Rossa, Lop, Herman, Liepmann, Hofmeier, and Offergeld. Moreover, it is interesting to note that the amniotic fluid frequently contains sugar, its presence having been demonstrated chemically in more than one-half the cases, while in some of the earlier ones its presence was indicated by the sweet taste and sticky consistency of the fluid. In the observations of Ludwig, Rossa, Herman, Hofmeier, and Offergeld quantitative determinations were also made and the amount of sugar was found to vary from 0.165 to 0.7 per cent. The fact that it disappeared from the urine of Rossa's patient shortly after delivery would apparently indicate that it was not a case of true diabetes, and accordingly it may be concluded that sugar may be present in the amniotic fluid in simple glycosuria as well as in diabetes.

Observations of this character are of interest not only in themselves, but also because they at one time seemed adapted to throw some light upon the vexed question of the origin of the amniotic fluid. At first they apparently indicated that it must be a transudate from the maternal blood, as the absence of sugar from the fœtal urine in several instances, as well as the fact that several other children were born in a macerated condition, indicated that their urinary secretion could not have contributed to the formation of the amniotic fluid. Unfortunately the observations of Chamberlent and Offergeld have shown that such conclusions are untenable, as the former demonstrated the existence of glycosuria in a child born of a diabetic mother, and the latter showed that both the blood and urine of an unborn child contained glucose, thereby raising the question whether the latter had been transmitted through the placenta or indicated the existence of fœtal diabetes.

Diagnosis. From what has already been said it is apparent that the mere reduction of Fehling's solution, upon which the practitioner ordinarily bases the diagnosis of diabetes, is open to many interpretations in the pregnant woman. Leaving out of consideration all substances other than sugar which may give rise to such a reaction, it may be obtained in as radically different conditions as lactosuria, the several varieties of glycosuria, and true diabetes. Accordingly the mere detection of the presence of sugar is of but little diagnostic or prognostic value, and as far as my experience goes has been pro-

ductive of quite as much harm as good, in that it frequently leads the incautious practitioner to diagnosticate the existence of diabetes with its comparatively sombre prognosis in patients who present a harmless lactosuria or glycosuria. That this is the case is shown by the fact that each year I receive letters from physicians in different parts of the country asking for advice in cases of supposed diabetes complicating pregnancy, which upon closer investigation have nearly always proved to be examples of transient glycosuria or lactosuria.

Therefore, whenever the presence of sugar is demonstrated in the urine of a pregnant woman, the first essential is to determine whether it occurs in the form of glucose or lactose. For practical purposes this is readily ascertained by the use of the fermentation saccharometer, as glucose ferments readily while lactose does not. If more accurate information is desired the characteristic glucosazone or lactosazone must be isolated, but unfortunately this latter procedure cannot be employed if quantitative results are desired. Moreover, it should be borne in mind that both glucose and lactose may occur together, and such a combination should be suspected whenever there is a discrepancy between the readings obtained by titration with Fehling's solution and by the use of the saccharometer, or when the polarimeter indicates the presence of a greater amount than the saccharometer.

If the sugar is definitely shown to be lactose, the condition must be regarded as lactosuria and may be dismissed from consideration as of no practical significance. On the other hand, if the presence of glucose is demonstrated the matter is not so simple, as it is then desirable to determine whether the patient is suffering from true diabetes or merely from transient or alimentary glycosuria. Unfortunately such a differentiation is by no means easy and frequently cannot be made without prolonged observation or knowledge of the previous history of the patient. If it be known that the glycosuria existed before conception the diagnosis of diabetes is assured, but if it were first detected during the course of pregnancy the interpretation is not so clear.

Generally speaking it may be said that a tentative diagnosis of diabetes is permissible whenever large amounts of glucose are present, or the patient presents characteristic symptoms; whereas transient or alimentary glycosuria should be suspected if the percentage of sugar is low and symptoms are absent. Such rules, however, are not absolute, as it sometimes happens that in the first class of cases the sugar and symptoms may permanently disappear after the delivery, while in the second the glycosuria may persist after labor and the characteristic symptoms of diabetes sooner or later may become manifest. This was clearly shown in Case VI, which was considered as transient glycosuria during pregnancy, and yet was shown to be true diabetes by the subsequent course of events.

Likewise the persistence or disappearance of sugar under dietetic treatment does not necessarily afford accurate information concerning the nature of the condition, as it sometimes happens, on the one hand, that cases of glycosuria will be uninfluenced by a carbohydrate-free diet, while, on the other hand, in true diabetes all trace of sugar may disappear temporarily under a plain milk diet, as was demonstrated in Cases II and III and Case VI, respectively.

The existence of alimentary glycosuria should be suspected in any case in which the sugar disappears from the urine upon the removal from the diet of certain saccharine substances, but without restricting the use of other carbohydrates. In view, however, of what has been said concerning the common factors in the etiology of transient glycosuria, it is manifest that it frequently will be impossible to differentiate between the two conditions.

PROGNOSIS AND TREATMENT. Unless the condition can be demonstrated to be either lactosuria or definite alimentary glycosuria, the presence of sugar in the urine of a pregnant woman should be regarded as a danger signal, and as an indication for continuous and careful observation. If diabetes be definitely diagnosticated from the previous history of the patient, the condition should be regarded as serious but by no means hopeless for either the mother or child, for as long as the patient presents no serious symptoms, acetone bodies are absent, and the output of sugar can be controlled by dietetic means, the prognosis may be regarded as favorable as far as the present pregnancy is concerned, and all that is necessary will be careful supervision. If, however, serious symptoms supervene, acetone bodies appear in the urine, or the output of sugar cannot be controlled by dietetic means, the condition should be considered as alarming and the pregnancy should be ended at once by the most appropriate means, as its continuance will add to the danger of the mother, while the child's prospects are so poor that they are not entitled to consideration. It is of course understood that the interruption of pregnancy will not cure the underlying disease, but it may nevertheless temporarily relieve the disordered metabolism from such a degree of strain as to enable nature to reassert herself and thus allow the patient to live for several years.

Most writers upon the subject advocate the induction of premature labor under the conditions just mentioned, although Vinay and Kleinwächter are absolutely opposed to it, while Graefe and Lesse believe that it is indicated only when the diabetes is complicated by hydramnios. Fellner, Schauta, and Senator and Kamminer hold that abortion is indicated in the early months provided the diagnosis is assured. Likewise the same line of treatment is indicated even if the existence of diabetes is not absolutely certain, but is rendered probable by the presence of large amounts of sugar or by the onset of threatening symptoms.

Tabulation of Cases of Diabetes Complicating Pregnancy.

A. Pregnancy Occurring in Diabetic Patients.

Author.	Date.	Age.	Para.	First symptoms.	Per cent. of sugar.	Pregnancy.	Labor.	Complications.	Child.	Mother.
1. Husband . . .	1874	26	III	Uncertain.	5.5	?	Spontaneous.	None.	Very small, lived several days.	Died 8 months later from tuberculosis.
2. Newman (*a*) . .	1876	36	II	Several years.	4.0	Uneventful.	"	"	Normal.	Diabetes continued.
3. Newman (*b*) . .	1876	36	III	Same patient as case (*a*).	4.0	"	Premature, sixth month.	"	Dead.	Died in coma third day.
4. Newman (*a*) . .	1878	32	m.p.	?	?	"	Spontaneous.	"	Normal.	Diabetes continued.
5. Newman (*b*) . .	1880	34	m.p.	Same patient as case (*a*).	?	"	"	"	"	Died in coma 2 years later.
6. Duncan . . .	1879	35	XI	Previous pregnancy.	Large.	Great thirst.	"	"	"	Died comatose 8 months later.
7. Reid	1880	32	II	Several years.	10.0	Thirst and diuresis	"	Hydramnios, fluid sticky.	Large, macerated.	Typical diabetes 2 years later.
8. Williams (*a*) . .	1880	?	I	?	?	Uneventful.	"	None.	Normal.	Sugar afterward.
9. Williams (*b*) . .	1881	?	II	Same patient as case (*a*).	2.0	"	"	Hydramnios, no sugar.	"	Diabetes continued.
10. Williams (*c*) . .	1881	?	III	Same patient as cases (*a*) and (*b*).	5.0	"	"	None.	"	Died 6 weeks later in coma.
11. Williams . . .	1882	36	VI	Uncertain.	Large am't	Thirst and diuresis	"	"	Macerated.	Died in coma 4 months later.
12. Duncan . . .	1882	30	V	Several years.	3.0	Uneventful.	Low forceps.	.....	"	Died third day after delivery in collapse.
13. Lecorché (*a*) . .	1885	?	?	Before pregnancy.	?	.....	Spontaneous.	.....	Normal.	Diabetes continued.
14. Lecorché (*b*) . .	1885	?	?	" "	?	.....	"	.....	"	" "
15. Lecorché (*c*) . .	1885	?	?	" "	?	.....	"	.....	"	" "
16. Lecorché (*d*) . .	1885	?	?	" "	?	.....	"	.....	"	" "
17. Lecorché (*e*) . .	1885	?	?	" "	?	.....	"	.....	Died second day.	" "
18. Lecorché . . .	1885	?	?	" "	?	.....	"	Premature rupture membranes	Normal.	" "
19. Lecorché . . .	1885	?	?	" "	?	.....	Premature.	Eighth month.	"	" "
20. Tarnier and Budin	1886	?	?	" "	Slight.	None.	Spontaneous.	None.	"	" "
21. Tarnier and Budin	1886	?	?	" "	5.0	"	Premature at six months.	.....	Dead.	Died in coma 3 hours later.
22. Warner (*a*) . .	1886	32	II	Second pregnancy	Definite.	Symptoms.	Spontaneous.	None.	Large, macerated.	Diabetes persists.
23. Warner (*b*) . .	1886	?	III	" "	"	"	"	Hydramnios.	" "	" "
24. Warner (*c*) . .	1886	?	IV	" "	"	"	"	None.	" "	" "
25. Warner (*d*) . .	1886	?	V	" "	"	"	"	"	" "	" "
26. Packard . . .	1889	41	m.p.	For years.	4.06	"	Repeated abortions.	.....	Abortion.	" "

27. Gaudard	1889	44	m.p.	For years.	Moderate.	Symptoms.	Spontaneous.	None.	Normal.	Diabetes persists.
28. Demelin	1890	?	?	?	?	Coma.	Died undelivered.	.....	Dead.	Died in labor.
29. Hehir	1892	32	?	2 years.	?	Symptoms.	Spontaneous.	Hydramnios.	Macerated.	Diabetes persists.
30. Seegen (*a*)	1893	?	?	Before pregnancy.	?	.....	Abortion.	Third month.	.....	Recovered.
31. Seegen (*b*)	1893	?	?	Same patient as case (*a*).	?	.....	"	"	.....	"
32. Seegen (*c*)	1893	?	?	Same patient as cases (*a*) and (*b*)	?	.....	"	"	.....	Died after last abortion.
33. Seegen (*a*)	1893	?	?	Before pregnancy.	5.7	.....	"	"	.....	Recovered.
34. Seegen (*b*)	1893	?	?	Same patient as case (*a*).	5.7	.....	"	"	.....	"
35. Seegen (*c*)	1893	?	?	Same patient as cases (*a*) and (*b*)	5.7	.....	"	"	.....	"
36. Ludwig	1895	42	IX	2½ years.	2.3	Uneventful.	Spontaneous.	Hydramnios.	Macerated.	Diabetes persists.
37. Graefe	1897	37	VI	2 years.	2.7	Coma.	Premature at seven months.	.....	"	"
38. Kleinwächter	1898	25	VI	1 year.	Definite.	Negative.	Spontaneous.	None.	Normal.	Alive, tuberculosis 7 weeks after last child.
39. Lop (*a*)	1899	?	VI	?	"	"	"	"	"	Diabetes persists.
40. Lop (*b*)	1899	?	VII	?	"	"	"	"	"	" "
41. Lop (*c*)	..	..	VIII	.....	"	"	"	"	"	" "
42. Lop (*d*)	..	..	IX	.....	"	"	"	"	"	" "
43. Lop (*e*)	..	..	X	.....	"	"	"	"	"	" "
44. Lop (*f*)	..	..	XI	.....	"	"	"	"	"	" "
45. Lop (*a*)	1899	?	IV	After third labor.	"	Uneventful.	"	"	"	" "
46. Lop (*b*)	..	..	V	" " "	"	"	"	"	"	" "
47. Lop (*c*)	..	..	VI	" " "	"	"	"	"	"	" "
48. Lop (*a*)	1899	?	II	After first labor.	"	"	"	"	"	" "
49. Lop (*b*)	..	..	III	" " "	"	"	"	"	"	" "
50. Lop	1899	?	III	After second labor	3.4	Premature labor at six months.	.....	Hydramnios.	Dead.	" "
51. Chamberlent	1901	31	IV	Before present pregnancy.	6.0 to 10.0	Uneventful.	Spontaneous.	Sugar in fœtal urine.	Normal.	" "
52. Liepmann	1903	30	VI	Before present pregnancy.	4.0	Hydramnios.	Induced labor at seven months.	Sugar in liquor amnii.	Dead.	Died ninth day, metritis dessicans.
53. Fels	1905	24	III	Six months before last pregnancy.	6.0	.....	Spontaneous.	None.	Normal.	Died 3 years later in coma.
54. Hofmeier	1906	33	VI	Just before last pregnancy.	3.5	Hydramnios.	Induced labor at seven months.	Sugar in liquor amnii.	Dead.	Died in coma fourth day.
55. Offergeld	1906	34	?	Some time.	4.85	"	Induced labor at six months.	Sugar in liquor amnii.	"	Diabetes persists.
56. Eshner	1907	37	II	3 years.	4.67	Negative.	Breech extraction.	Coma.	Macerated.	" "
57. Chapiet	1907	?	VI	Last pregnancy.	Large.	Intense thirst.	Forceps.	Hydramnios.	"	Died 9 months later from tuberculosis.

57 pregnancies in 34 women: gross mortality, 24.58%; during labor and puerperium, 12.29%; children alive, 50.88%; born dead, 36.88%; aborted, 12.24%.

B. Diabetes Developing during Pregnancy.

Author.	Date.	Age.	Para.	First symptoms.	Per cent. of sugar.	Pregnancy.	Labor.	Complications.	Child.	Mother.
58. Duncan . . .	1871	30	III	Early in pregnancy.	Large.	Emaciation, amaurosis.	Accouchment force.	.....	Macerated.	Died in coma third day
59. Winckel . . .	1874	?	?	Day of labor.	"	Normal.	Slow.	Hydramnios.	Normal.	Sugar on discharge thirteenth day.
60. Loeb	1881	22	?	Second month.	4.0	Symptoms.	Abortion at six months.	.....	Dead.	Died 1 month later.
61. Davidson . . .	1882	38	IV	Middle of pregnancy.	10.0	Thirst, emaciation	Spontaneous, premature.	None.	Died 13 hours.	Died in coma 4 months later.
62. Frerichs . . .	1882	36	X	Eighth month.	?	Normal.	Normal.	"	Normal.	Death 15 months later, phthisis, brain tumor.
63. Fry	1891	31	II	Fourth month.	3.0 to 6.0	Symptoms.	Premature.	"	Macerated.	Died in coma 3 days later
64. Born	1892	24	I	Seventh month.	8.5	"	Died in coma undelivered at seven months.	.....	Dead.	Died in coma.
65. Taylor . . .	1897	31	II	Sixth month.	8.5	No symptoms.	Normal.	None.	Normal.	Diabetes persists.
66. Herman . . .	1902	30	VII	Third month.	2.0 to 3.0	Comatose.	Premature.	Hydramnios.	Macerated.	Died ninth day, sarcoma of lung.

9 pregnancies in 9 women: 78% maternal mortality; 45% in first ten days; 33% one to fifteen months later; 66.67% fœtal mortality.

C. Doubtful Cases of Diabetes Complicating Pregnancy. Sugar Disappeared after Delivery.

Author.	Date.	Age.	Para.	First symptoms.	Per cent. of sugar.	Pregnancy.	Labor.	Complications.	Child.	Mother.
67. Bennewitz (*a*)	1826	22	IV	This pregnancy.	?	Intense thirst.	Spontaneous.	None.	Normal.	Sugar disappeared.
68. Bennewitz (*b*)	1826	?	V	Early.	12.0	" "	Operation.	Threatened coma.	Dead, 12 lbs.	Perfect recovery.
69. Bennewitz (*c*)	1826	?	II	.....	?	" "	Spontaneous.	None.	Normal.	" "
70. Williams	1882	33	VII	?	Consid'able	Emaciation.	Face, forceps.	Perineal tear.	"	Sugar disappeared 5 months later.
71. Marcus	1892	27	I	Puerperium.	0.7	None.	Forceps.	Decubitus.	"	Disappeared in 6 weeks.
72. Trouillard	1893	28	III	Early in pregnancy.	?	Thirst, somnolence	Abortion.	Twins at five months.	Dead.	Perfect recovery.
73. Partridge	1895	20	I	Fourth month.	3.0	Marked symptoms	Spontaneous.	Albuminuria.	Normal.	No sugar for next 2 years
74. Taylor	1897	39	m.p.	Seventh month.	0.75	No symptoms.	"	None.	"	No sugar after labor.
75. Rouff (*a*)	1903	25	II	This pregnancy.	4.0	Pruritis.	Version.	Hydramnios.	Lived 12 hours.	Gradually disappeared.
76. Rouff (*b*)	1903	25	IV	Fourth month.	?	Slight symptoms.	Forceps.	.....	Dead.	Disappeared after delivery.
77. Rouff (*c*)	1903	25	V	Onset of pregnancy.	5.0 to 7.0	Marked symptoms	Induced labor at eight months.	.....	Lived 3 months.	Disappeared permanently
78. Stengel	1904	33	II	Sixth month.	5.0	Hunger and thirst	Spontaneous.	None.	Normal.	" "
79. Durieux	1905	37	III	Seventh month.	Large am't	Intense thirst.	"	Rigorous diet.	"	" "
80. Tate (*a*)	1906	33	II	Third month, second pregnancy.	Consid'able	Pruritis, thirst.	Abortion at four months.	.....	Dead.	Disappeared 4 weeks later.
81. Tate (*b*)	1906	35	III	Third month, third pregnancy.	Present.	" "	Spontaneous.	None.	Normal.	Disappeared later.

15 pregnancies in 10 women: no maternal deaths; 12 labors at term; 1 premature labor; 2 abortions; 10 live children (75 per cent.).

On the other hand, it should be remembered that in the vast majority of cases the presence of sugar is not indicative of the existence of diabetes, but merely of transient or alimentary glycosuria, and the latter diagnosis should be made tentatively whenever the amount of glucose does not exceed 2 or 3 per cent. and symptoms are absent or only slightly marked. In such cases the urine should be examined at frequent intervals and the amount of sugar excreted in the twenty-four hours definitely determined. As long as it remains stationary or can be controlled by dietetic measures, the prognosis should be regarded as favorable and there should be no thought of interfering with the pregnancy.

In view of the fact that many cases of mild diabetes have no deleterious effect upon the course of pregnancy and labor, such an outcome should not be taken to indicate that the condition is merely simple glycosuria; but the urine should be examined at varying intervals following delivery and diabetes should be diagnosticated if sugar is persistently present, whereas if repeated examinations show that it has disappeared, such a diagnosis is not justified no matter what its percentage may have been during pregnancy or by what symptoms it may have been accompanied.

CONCLUSIONS. 1. A positive reaction with Fehling's solution during pregnancy does not necessarily indicate the existence of diabetes, but is usually due to lactosuria or to transient, alimentary, or recurrent glycosuria.

2. In such cases it is imperative to determine whether the sugar occurs as lactose or glucose, as lactosuria is without clinical significance and is probably associated with premature activity of the breasts.

3. The significance of glycosuria is not so clear. If alimentary in character it may be regarded with impunity. Otherwise it may be of the transient or recurrent variety, or may indicate the existence of true diabetes.

4. If the glycosuria appears late in pregnancy, does not exceed 2 per cent. in amount and is not accompanied by symptoms, it is probably transient and may disappear spontaneously at any time or persist until the end of pregnancy. In either event it is usually of slight clinical significance, and merely indicates that the patient should be carefully watched.

5. If the sugar appears early in pregnancy and in large amounts the condition is more serious, as it may be impossible to make a positive diagnosis until after delivery, when the condition disappears in glycosuric but persists in diabetic cases.

6. Pregnancy may occur in diabetic women or diabetes may become manifest during pregnancy. Either is a serious complication, although the prognosis is not so alarming as is frequently stated; many patients do perfectly well, while a smaller proportion die in coma or collapse at the end of pregnancy, or during or shortly after labor.

7. If the output of sugar is large and cannot be controlled, or at least markedly diminished by suitable dietetic and medicinal treatment, the induction of abortion or premature labor is indicated even in the absence of serious symptoms, and much more so when they are present.

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MEDICAL GYMNASTICS IN EARLY MYOCARDIAL INCOMPETENCE WITHOUT VALVULAR DISEASE.

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There is a large and important group of cardiopathies which is encountered among business men, and which furnishes such a great contingent to the increasing number of deaths from heart disease as to call for preventive and therapeutic measures. The cases referred to are found especially among men of affairs who, in response to the demands of modern commercial methods, lead very strenuous lives. The high tension under which professional and business men work nowadays is, of course, not the only, nor perhaps the chief, factor in producing myocardial incompetence, but it contributes powerfully to this end, no doubt. We may never be able to discover the cause or causes in more than a general way, as at present, and, moreover, we must not ignore the role played by acute and chronic infections in the etiology of cardiovascular degenerations, but in studying the class of cases that form the subject of this paper, with a view to therapy as well as etiology, it will be well to bear in mind the teachings of pathology.

The cardiopaths now considered are generally men of large physique, who, in addition to an occupation necessitating many hours daily at the office desk or in the counting room, are generous livers and often heavy smokers. Accordingly they take on weight, and very commonly display an abdominal girth out of proportion to their chest measurements. In a proportion of the cases these men, endowed with a magnificent physique, have been athletes in college, but on entering professional or commercial life have neglected physical exercise because of the ardor with which they devote their energies to their chosen careers. In the majority of instances these individuals possess indomitable energy and almost tireless activity, and display a systolic blood pressure that is well up toward, if not actually above, normal limits. Such, in the main, are the physical makeup and business conditions of these men who, in the late fifties or early sixties, consult us for symptoms which betoken long-endured and at length injurious cardiac strain.

Regarding the pathology of these cases, it need only be pointed out that the whole cardiovascular system is a sufferer, though not uniformly. The kidneys, too, participate in this degenerative process, but in the cases especially referred to in this paper, renal inadequacy is not marked and is overshadowed by that of the heart. The coronaries do not escape, but only occasionally are so involved as to occasion the symptoms of angina pectoris. The heart muscle

is the portion of the circulatory apparatus which first forces its functional disturbance upon the notice of the individual. Yet it has not been the first to feel the injurious effects of those various factors that are bound, in time, to bring disaster, for, as Hasenfeld and others have shown, the degenerative process begins in the intra-abdominal vessels, which are under the immediate control of the splanchnic nerves. There is persistent increase of blood pressure within this area, and, secondarily, throughout the entire vascular system. Strain on the myocardium results, and this enormous peripheral resistance, augmented by the strenuous and luxurious conditions of modern city life, wear out the heart prematurely.

Whatever may be all the factors or the precise modus operandi, I was impressed years ago by the clinical observation pointed out by Fraentsel in his classic description of what he termed idiopathic enlargement of the heart, namely, the frequency of myocardial incompetence in men of impressive abdominal girth and large physique, who spend their business hours in their office chairs and take altogether too little exercise in proportion to their consumption of food.

Therefore, in reflecting upon these various considerations, pathological and etiological, I came to the very natural conclusion that if the heart were to be strengthened, it would have to be relieved of some of its load, and not merely whipped on by digitalis. In other words, the peripheral resistance existing in the sluggish circulation within the mesenteric vessels should be lessened. That is, since these individuals sit too long, and their hearts are deprived of the aid that comes from muscular exercise and deepened respiration, they should endeavor to counteract this injurious tendency.

The foregoing reflections led me to the belief several years ago that in the early stage of myocardial incompetence the rational therapy lay in such means as was most likely to counteract the primary circulatory condition conceived to underlie the cardiac hypertrophy. Accordingly I began to send men of the type described to a medical gymnast, to whom was explained the end to be attained. He comprehended my purpose, and, being familiar with the investigations of Levin, subjected the patients to a course of gymnastics of the kind studied by Levin. This investigator showed, by a record of 600 pulse readings, that if certain simple exercises were given properly, they were capable of *slowing* and *strengthening* the pulse, instead of accelerating it, a *very vital principle* in the class of cases here considered.

The medical gymnastics consist of both active and passive movements, according to the degree of myocardial incompetence present. The former comprise certain rolling and bending movements of the trunk executed by the gymnast, who, standing behind the individual seated on a wooden horse, with his feet held firmly by toe-straps,

grasps the shoulders and firmly yet not too vigorously bends the body forward and then rolls it around to the opposite side in a backward direction, in such a manner that, flexed in the beginning, the trunk becomes extended when the movement is half completed, and ends again in a position of strong flexion. To these may be added passive flexion and extension of the extreities, and alternate expansion and compression of the chest, very much after the manner of performing artificial respiration.

The active exercises, which in all cases are gentle at first, and performed by the help of the gymnast, and only by degrees increase in vigor, consist in deep breathing, in bending, pulling, lifting, etc., on a horizontal bar or ladder, or such other movements as in the judgment of the gymnast will promote respiration and venous flow and reduce the girth of the abdomen.

But whatever be the kind of exercises, one essential principle underlies them all, namely, *the patient must not be allowed to hold his breath, but must breathe regularly and deeply in rhythm with the movements*, so as to inspire or expire according as the exercises expand or contract the chest, and depress or raise the diaphragm. It is this rhythmical breathing which the gymnast must watch carefully, for it is found that so soon as the individual holds his breath his face becomes congested and his pulse accelerated; whereas, if respiration is carried on regularly, the opposite effect is produced. Lastly, the gymnast keeps close watch of the pulse, and whenever it is observed to show acceleration and diminished volume the individual is made to rest or to breathe deeply in such a manner as will improve pulse rate and volume.

The purpose of these exercises is not the development of the skeletal muscles, but the restoration of the functional integrity of the myocardium, and this they accomplish more or less effectively, not only by increasing venous flow on the one side, and by dilating the intermuscular arterioles on the other, but also by improving cardiac metabolism. This last is the result of several factors. In the first place, the circulation within the coronary vessels is improved, for with more efficient systoles the coronary veins are more fully emptied and the heart muscle receives a greater supply of arterial blood. This direct effect upon coronary circulation is enhanced by the improved flow in the pulmonary vessels, and consequently a better oxygenation of the blood supplied to the myocardium, while the correction of a tendency to stasis within the right auricle removes any impediment to outflow from the coronary veins and lymphatics into the auricle occasioned by overfilling of its cavity. From whatever standpoint, therefore, we contemplate the effect of these gymnastics, we see they must be theoretically, if not practically, beneficial.

This brings us to the query: Do the results bear out the theory, and how great and how lasting is the improvement? It is not

practical to report cases in response to this query, and hence it must suffice if the subjective and objective effects are stated.

Of course, the degree and permanence of the improvement must depend largely upon the state of the heart muscle. If this is extensively degenerated, no amount or kind of treatment can be expected to achieve much, and such improvement as is gained cannot last long. In such cases, therefore, if dilatation and inadequacy are pronounced, the so-called resistance exercises are preferable, although to these may be added with advantage such deep breathing movements as, with the aid of a trained attendant, can be performed without danger of strain to the heart wall.

As might be expected, the most pronounced benefit has been observed in cases of early or moderate myocardial incompetence, shown by breathlessness or palpitation upon slight cause, and upon examination by increased cardiac dulness, feebleness of the first tone at the apex, accentuation of the pulmonic second sound, and sometimes a faint systolic whiff in the mitral area. In most, but not all, cases the blood pressure is elevated above the normal. In such cases the first indication of improvement is shown by greater ease of respiration and a general sense of ease or lightness. Energy is increased and fatigue comes less easily, while a better action of the bowels and a diminution of waist measure are quite generally observed. These subjective indications of improvement have been especially and repeatedly marked in a man, aged fifty-nine years, with stiff arteries, a systolic blood pressure of 225 (broad arm band), and a greatly hypertrophied, habitually accelerated heart. After a month's treatment he is generally quite ready to cease the exercises, because satisfied with the improvement. Indeed, one of the difficulties met with has been the convincing of the patients of the wisdom of a continuance of the treatment with a view to preventing the return of the symptoms.

Objectively, it is noted at the time of the exercises that the pulse slows and its quality improves, provided the movements are properly directed by the assistant, and the breathing is carried on regularly, as already stated. Consequently it is of the utmost importance that these exercises be controlled by a trained assistant, and that the individual be forbidden the performance of so-called self-resisting exercises at his home.

The effect is thus seen to be quite different from that of ordinary physical exertion, which, when the myocardium is damaged, causes acceleration of the heart's action without subsequent rise of blood pressure as the heart resumes its wonted rate. This lack of recovery (Graupner's Erholung) is a sign of cardiac weakness, and in the class of cases here considered it is not desirable to have the myocardium subjected to such a degree of strain. Accordingly, it is important that these medical gymnastics be given by an assistant who understands the kind of exercises which slow and strengthen the

pulse, and will maintain a careful watch over the pulse and color of the skin, in order to detect the earliest signs of cardiac strain.

To make matters doubly sure, it is my wont to examine the patients directly after the first one or two seances, and thereafter once a week.

If the myocardium is susceptible of improvement, this is shown by decrease in the area of dulness, especially on the right, added strength and clearness of the heart tones, and often by the disappearance of the systolic whiff of muscular mitral incompetence previously heard at the apex. Almost without exception the results observed have been gratifying, and have justified the recommendation of this plan of therapy.

In some cases there has been a small amount of medication, either in way of preparation for this gymnastic treatment, or to assist in more speedily and surely restoring cardiac efficiency. The medicinal therapy has consisted in occasional cathartics, a vasodilator, as nitrite of sodium, strophanthin, digitalin, etc., but in all truth it may be said that the medical gymnastics have been the main agent in the accomplishment of the results noted. Indeed, so much pleased have I been that I seldom nowadays prescribe the so-called resistance exercises of Schott, because, even when the heart may be too feeble to endure anything more than deep breathing in the manner described, this seems to me fully as efficient, in conjunction with other measures, as are the Schott movements.

In conclusion, my experience with medical gymnastics in cases showing early incompetence of the myocardium warrants me in recommending them, if properly controlled, and in asserting the belief that, if these and allied physical exercises were used more extensively and systematically by men of the build and habits to develop chronic myocardial and arterial disease, they would delay, if not prevent, the onset of cardiac inadequacy.

THE VALUE OF THE INUNCTION METHOD OF ADMINISTERING DRUGS TO CHILDREN.

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In 1894[1] and in 1901[2] I published papers on the value of inunctions of guaiacol in the treatment of tuberculosis in infants and children. Since my first publication on this subject, fourteen years

[1] Ohio Med. Jour., May, 1894.

[2] Archives of Pediatrics, May, 1901.

ago, I have continued to use this treatment daily in hospital and private practice, and my long experience with it has confirmed my earlier views that guaiacol, when administered in this way, is the most valuable medical remedy we have in the treatment of this disease.

My experience with inunctions of guaiacol during these years has increased my interest in this method of administering drugs to young children, and has led me gradually to the belief that a number of other drugs may be more advantageously administered by inunction than by the mouth, and that especially in young children a number of diseases, such as hereditary syphilis, infantile tuberculosis, and respiratory diseases, such as bronchitis and pneumonia, can in most instances be more readily influenced by medicines given by inunction than they can be by medicines given by the mouth, even if the latter mode of administration did not disturb the functions of the gastro-intestinal tract. Cushny says: "The great mass of drugs absorbed from the stomach and intestines is carried to the liver before reaching the general circulation, and this is of great importance in determining their effects in the body, as some of them are retained in that organ, and are either entirely destroyed or escape so slowly that they have no perceptible effect." This objection does not apply to drugs that are given by inunction, since the liver is not interposed between their point of absorption and the lymphatic and general circulation.

It is apparent, therefore, that all drugs which favorably influence lymphatic disease and which can be introduced by inunction will be much more efficacious when given in this way; and it is also apparent, especially in young children, that all drugs which can be administered by inunction, and which are intended to influence favorably diseased processes in the blood, in the respiratory passages, or at the point of excretion of the various drugs, should preferably be administered in this manner rather than by the mouth.

These views prompted me to make certain experiments bearing upon the absorption of medicines given by inunction, and have led me to the presentation of this paper, which deals specifically with this form of administering certain drugs for the purpose of combating certain diseases in infants and young children.

Inunctions are very much more efficacious for the treatment of disease in young children than they are in adults, for the following reasons:

1. In infants the surface of the skin in proportion to the body weight is four times greater than it is in adults. This brings the whole blood and lymph circulation of the infant in close communication with the bloodvessels and lymphatics of the skin and makes it possible for drugs which are rubbed into the skin to pass quickly through the body and make their appearance in the urine, feces, bronchial mucus, and other excretions.

2. In infants the vasomotor mechanism is much more responsive to reflex stimuli than it is in adults, and for this reason the capillary circulation in the skin of the infant is made much more active by the application of heat and friction, as in the giving of inunctions. This facilitates the absorption of the inunction and the ready introduction of medicines into the general circulation.

3. All lymphatic structures are functionally more active in the young child than in the adult, and the lymphatic circulation in the skin and in other parts of the body is relatively more active and functionally more important than it is in the adult. This facilitates the absorption of inunctions and makes possible the ready introduction of medicines through the skin into the lymphatic circulation.

4. In young children, and especially in infants, the nutritional problems in the treatment of all diseases are of vastly greater importance than they are in the adult, and it is, therefore, of the utmost importance that the stomach and intestinal canal should be kept in the best possible condition; consequently all drugs that can be advantageously administered in some other manner should be kept out of the stomach. This is especially true of drugs that are intended to influence general metabolism and to act upon diseased tissues remote from the gastro-intestinal canal.

5. The diseases which can be reached most readily by inunctions, such as diseases of lymphatic strutures and of the respiratory passages, are much more common and much more severe in young children than they are in adults, which facts very much enhance the relative importance of the inunction treatment in young children.

6. Experiments demonstrate that certain medicines may be introduced with great facility, by inunctions through the skin, into the circulating media of the body, and that this result is more readily accomplished in infants and young children than it is in adults.

In my experiments I used guaiacol, iodine, oil of wintergreen, and salicylic acid. These medicines, with the exception of the iodine, were combined with anhydrous lanolin in the proportion of one dram to the ounce. The iodine used was a 6 per cent. iodine-vasogen. In adults stronger ointments, two drams to the ounce, were employed.

In applying the ointments the following technique was observed: The skin of the chest and abdomen was carefully washed with soap and warm water, and hot, moist towels were then applied for a few moments to warm and redden the skin. One dram of the ointment was then very carefully and gently rubbed into the skin of the chest and upper part of the abdomen. The inunction was continued for from five to ten minutes. Previous to the inunction the child's bladder had been emptied, and directions were then given to save all urine passed. If at the end of two hours no urine was obtained the bladder was emptied by catheterization, and subsequent specimens of urine were also saved for examination. The urine thus

obtained was examined to determine the presence or absence of the drug which had been administered by inunction.

By this method the following results were obtained: Eight children under seven years of age were rubbed with oil of wintergreen, and in every instance the drug was found in the urine within two hours after rubbing. It was observed that in the younger children, some of whom were less than a year of age, the reaction in the urine occurred earlier, in one instance within an hour and one-half, so that, on the whole, it may be said that the younger the child the earlier the reaction; if a definite time limit was observed the reaction was stronger in the younger children.

The reaction could also be obtained in the adult by using twice or three times the quantity of oil of wintergreen and applying the inunction for a longer time. This was true also in the inunction experiments with the other drugs, so that I think it may be definitely stated that the urinary reaction showing the presence of the drug could always be obtained in the adult if a larger dosage and longer and more vigorous rubbing were resorted to, but even under these conditions the reaction in the adult urine was not as pronounced as it was in the infant.

As an example let me cite the following experiment: R. S., aged four years, weight 28½ pounds. Oil of wintergreen inunction at 1 P.M. One dram of the ointment used; the inunction lasted five minutes. At 3 P.M. the urine showed rather faint traces of the drug; at 5 P.M. the reaction was much more marked; at 10.30 P.M. it was very well marked, and a second inunction was given at this time. At 1 A.M. the reaction was much more intense. This experiment shows the gradual increased elimination of the drug for five or six hours after the inunction, and also that under repeated inunctions the reaction becomes more and more intense.

Salicylic acid was used by inunction in five children under nine years of age, in all of whom the drug was found in the urine within three hours after the inunctions. It was thought that the reaction from salicylic acid appeared in the urine almost if not quite as readily as it did from the oil of wintergreen. Salicylic acid was also found in the urine of two adults who were rubbed with larger quantities for a longer time.

Guaiacol was used by inunction in 14 children and 8 adults. In all the children positive reactions were obtained in the urines within two hours. In two of the younger ones the reaction was obtained within an hour and one-half. In 4 of the adults a negative reaction was obtained after two, three, and four hours, but in these only one dram of the guaiacol ointment was used. In the other 4 adults two or three drams of the ointment were used and the inunction was applied for a longer time. In all of these a positive reaction was obtained within three and one-half hours.

Iodine was used by inunction in 6 children and 3 adults, in all of

whom a positive reaction in the urine was obtained within two hours. With the children one dram of the iodine-vasogen was used, and the inunction was applied for from five to eight minutes. In the adults two or three drams was used and the inunction was applied for ten or fifteen minutes.

These experiments demonstrate the practicability of administering by inunction to infants and young children guaiacol, salicylic acid, oil of wintergreen, and iodine, and they also show that this method of administering medicines is probably more efficacious in children than it is in adults.

Oils by Inunction. Almost from the beginning of the history of medicine the general profession as well as the laity has had great faith in the restorative power of inunctions of oil. And at the present time our faith in oil inunctions is almost as great as at any other period in the history of medicine. This faith, founded on empiricism and supported by countless clinical observations, is perhaps as firmly grounded as most of our ideas concerning the medical treatment of disease. There can be little doubt that lanolin, lard, codliver oil, and other fats may be introduced by inunction through the skin of the infant in sufficient quantities to aid materially the nutritional processes. This method of administering fats is of real value in very young children suffering from chronic nutritional disturbances, whose gastro-intestinal canal forbids the administration of fats by this channel in sufficient quantities to supply nutritional demands.

Guaiacol mixed with anhydrous lanolin in the proportion of one dram to the ounce, when administered to young children, as noted in the above experiments, quickly enters the lymphatic and general circulation and, compassing every part of the body, passes to the beginning of its excretion in the urine within two hours. This fact makes guaiacol, administered in this manner, a valuable remedy in certain diseases: (1) When a general or local lymphatic antiseptic is indicated, as in lymphatic tuberculosis and tubercular peritonitis; (2) in streptococcic and other localized infections of lymphatic tissues, as in non-tuberculous enlargements of the lymphatics of the neck and other parts of the body; (3) in pulmonary tuberculosis and in all diseases in which a pulmonary and bronchial antiseptic is indicated, as in the various forms of bronchitis, pneumonia, and other diseases of the respiratory tract in infants.

For many years I have followed the plan of treating influenza, bronchitis, and all the milder affections of the respiratory tract in infants with guaiacol inunctions to the exclusion of almost every other form of medication intended to influence by internal administration local conditions in the lungs or bronchial tubes. In other words guaiacol has taken the place of all expectorants, including the ammonia preparations, squills, ipecac, and other drugs of this class,

and even in the treatment of bronchopneumonia and lobar pneumonia in the infant guaiacol inunctions have formed an important part of the routine treatment.

I have long been convinced that the routine treatment of bronchial and pulmonary infections in infants, as outlined by our best authorities, which includes the use of such medicines as ammonia, squills, and ipecac, is responsible for no small part of the mortality in these diseases. The substitution, therefore, of guaiacol by inunction for expectorants which destroy the appetite and digestion of young children is of the greatest possible importance as a life-saving measure in the treatment of all bronchopulmonary diseases. It follows, of course, without saying that other rational lines of medication and measures of treatment now in vogue and which do not disturb the stomach are to be continued in connection with the guaiacol treatment of these diseases.

I am prepared to assert that guaiacol given in this way over a long period of time can do no harm. I am sure that I have prescribed it more than a thousand times in the last fifteen years, and I have never seen any ill effects from its use. I have given it in the above dosage to frail and malnourished infants for months at a time, and have seen only good result from its long-continued use.

Iodine by inunction is a rapid and efficacious way of administering iodine to infants and young children for all those conditions in which iodine or the iodides are indicated. This method of administering iodine is especially valuable, since it is almost impossible to give it or any of its combinations to infants by the mouth without producing more harm by upsetting the stomach and interfering with the digestive processes than the possible good which may result from its administration by the mouth. Iodine administered by inunction is of positive value in the treatment of late syphilis, of chronic glandular enlargements, of some acute catarrhal conditions of the bronchial mucous membranes, and as a general alterative in certain forms of chronic malnutrition.

Oil of wintergreen by inunction is a valuable way of introducing this drug into the general circulation in infants and young children. The indications for its use are to be found in all those conditions in which it is necessary to give the salicylates for their influence upon diseased conditions outside of the intestinal canal. In lumbago, acute and chronic rheumatism, chorea, tonsillitis, and endocarditis the salicylates are valuable, and in these and other conditions in which the salicylates are indicated, as good or better therapeutic results can be obtained in infants by inunction of the oil of wintergreen as by giving the salicylates internally. It is evident that by this method the child will be saved from the gastro-intestinal disturbances and consequent interference with nutrition, which so commonly follow the administration of this drug by the mouth. If it be preferred, salicylic acid combined with anhydrous lanolin may

be administered by inunction instead of the oil of wintergreen, as it is absorbed almost as readily.

Mercury by Inunction. This method of giving mercury to infants and young children in the treatment of syphilis is so fully recognized by the profession as being superior to any other method of administration that I do not feel called upon here to more than mention the fact.

Colloidal silver within the past few years has been administered hyperdermically, by the stomach, and by inunction in the treatment of various forms of localized and general septicemia. The profession, as a whole, I think, has come to recognize that this is a most valuable adjunct in our teatment of septicemia, and I for one, after a large experience extending over quite a number of years, am firmly convinced of its efficacy. In the acute enlargement of the lymphatic tissues of the neck which may follow scarlatinal, diphtheritic, and other forms of tonsillitis I believe that this remedy, in the form of unguentum Credé, properly rubbed into the surrounding lymphatic tissues, is of very great value in preventing the spread of the disease and in controlling the localized sepsis. This drug can be given more efficaciously to infants and young children by inunction than in any other manner, and its value in combating general and localized sepsis is of much more value in infants and children than it is in adults, because inunctions in general, are, for the reasons given in the early part of this paper, more efficacious in children than they are in adults.

THE TREATMENT OF IRREDUCIBLE CONGENITAL LUXATIONS OF THE HIP BY OPERATIVE MEANS.

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The treatment of congenital luxations of the hip by the bloodless method of reduction has so occupied the attention of the profession for many years past, that it may be well to recall what can be done for the relief of those cases which have passed beyond the period when it is possible to reduce the luxation by non-operative procedures. Many such patients pass their earlier years with comparatively little pain, and, notwithstanding their deformity and more or less disability, do not apply for treatment until pain and difficulty of locomotion demand relief. The histories of several cases are briefly as follows:

Case I.—Jessie V., aged fifteen years, was admitted to the Orthopedic Hospital, October, 1904, with double congenital luxa-

tion of the hips. While both hips were out only the left one was causing complaint. The right one seemed firmly applied to the ilium and did not appear to move in walking. The left one, however, shifted its position markedly. It was quite loose and the left limb was 3 cm. shorter than the right. There was a marked waddling gait and pain which caused her to apply for relief. She was put to bed and weights amounting to fifteen pounds applied for about six weeks. In December, 1904, she was etherized and an unsuccessful attempt was made at reduction by the ordinary circumduction method. Hyperextension over König's padded block was also tried without result. A heavy, wide, close-fitting belt of webbing with a pad and perineal straps was then applied; this afforded some relief and she left the hospital.

In February, 1906, two years later, she was re-admitted with her condition much aggravated. Pain was almost constant, walking for any distance was impossible, and she was unable to earn her living. Her charitable friends were then looking around for some place where she could be taken care of. She was again put on extension and again an unsuccessful attempt was made at reduction. This failing, in April, 1906, she was operated on. An anterior incision was made, a new socket was excavated from the ilium above the old acetabulum, the head of the femur was inserted therein, and the limb was put up in plaster-of-Paris in an abducted position. She was kept abed for eight weeks and then allowed to get up with a cast on. This was removed one month later and in another month she was walking well with the aid of a cane. She was then discharged. Since that time she has improved. While she still has a somewhat peculiar gait she can walk long distances without pain. The hip is movable in all directions, but does not slide up and down; it has evidently retained its position in its new acetabulum. She was formerly unable to take exercise and grew fat and very heavy; now she is active, working, and earning her living, and has lost the excessive fat and weight which previously encumbered her. The transition from her previous helpless condition to her present active and useful one has been very marked.

Case II.—Minnie H., aged sixteen years, was under treatment in 1892 by another surgeon for some deformity of the feet, the exact character of which is not known. It was stated by the nurse that when an infant the child had paralysis of both lower extremities. Tenotomy of both Achilles tendons was done and later braces were applied and worn continuously thereafter.

In 1897 she came under my care. At that time there was marked paralysis of both lower extremities together with double congenital luxations of the hip. Locomotion was almost impossible. One foot was in marked paralytic valgus, while the other was more of a paralytic equino varus. The left hip was luxated anteriorly, while the right was luxated posteriorly. An arthrodesis was done

on the right foot, which improved its position somewhat. The right hip was then operated on by an incision over the trochanter; the ligamentum teres was removed and the adductors and tensor fasciæ femoris divided subcutaneously. The head was brought down to the acetabulum, but as it would not stay in place a new acetabulum was excavated. The child was markedly strumous and long-continued suppuration followed this operation. It did not involve the deep parts around the bones but rather the superficial parts, so that while very extensive scarring resulted the hip region was not at all stiffened and movements were not restricted. After two months, however, she got up with a brace and she was able to get around some, but dragged especially her left leg. Nothing was done to the left hip, which remained fairly well in its displaced position with the head just below the anterior superior spine and the trochanter posterior; evidently there was a twisting of the neck and shaft.

She again applied for treatment in 1906, nine years after the previous operation. On examination the right hip was found to have again become luxated on the dorsum of the ilium. The left hip was apparently somewhat more posterior. The right hip slid up and down from one-half to one inch. In April, 1907 (thirteen months ago), the right hip was again operated on, a new acetabulum was dug out and the head inserted and the limb put up in the abducted position in plaster-of-Paris. Healing was uneventful. To correct the dropping down and in of the anterior part of the right foot the tibialis posticus, extensor proprius hallucis, and peroneus brevis were loosened and attached to the extensor longus digitorum. The distal end of the extensor proprius hallucis was attached to the tendon of the adjoining toe. On the left foot the peroneus brevis tendon was attached to the tibialis anticus, as were also the extensor tendons of the fourth and fifth toes. The distal ends of these tendons were sutured to the tendons of the second and third toes. After about twelve weeks the patient got around. Stout shoes were ordered to hold the feet firmly and a corset to support the trunk.

At present, one year after operating, she walks without cane or crutch. She has a marked paralytic eversion of the left foot with evident twist in the bones. An apparatus might be constructed to hold this foot inward, but it would have to extend from the pelvis to the foot and this she declines to wear. The hip is firm in place and movable functionally, and gives her no trouble.

Case III.—Miss C., aged twenty years, had a congenital luxation of the left hip. She limped, but not excessively. About five years previously while walking the joint seemed to catch; since then it has ached and the pain has become so constant as to induce her to seek relief. She was operated on in conjunction with my colleague, Dr. Taylor. An anterior incision was made as in the other cases, and a place was cleared in a depression in front of the former

location and above the acetabulum, but no bone was removed. The limb was put up in plaster in abduction. At present, over a year after the operation, she walks excellently. There is no slipping of the head of the femur, and with a half inch added to the heel she is comfortable unless she unduly exerts herself, when she experiences a feeling of weakness.

These cases represent some of the worst in the domain of surgery. When a person is young, say under ten years of age, the dislocated hip can usually be replaced without a cutting procedure, but after that age attempts at reduction are apt to fail and other means have to be resorted to. Some surgeons do not regard an unreduced congenital luxation as being very serious. My experience has been different. In almost every case a greater or less amount of disability occurs in later life, in addition to the awkward gait and limited use of the affected joint inseparable from the affection. Only recently have I seen a woman, aged fifty-five years, again disabled by pains in the affected hip.

A dislocated hip is an unreliable hip that is certain to give rise to serious trouble in some portion of the patient's life. These congenital luxations can usually be reduced by the bloodless method up to about the age of ten years. Later in most of the cases it is impossible to restore the head to its socket and one is, therefore, forced to seek a new position for the head of the femur to rest in.

The treatment of congenital hip luxations has developed on two separate lines: the non-operative and the operative. It began about 1826 when Dupuytren brought forward his pelvic band. Corsets, jackets, and braces followed. The next advance was about in 1847 when Humbert, and especially Pravaz, of Lyons, advocated traction to bring the hip down and then pushing it over into place. This method was followed in a more or less modified form by Buckminster Brown, Bradford, Mikulicz, Max Schede, and others. While these traction methods were being developed, other surgeons were doing operations for the same condition.

Guerin was one of the first to cut the muscles subcutaneously; Brodhurst and others followed. Resection of the displaced head was given quite a thorough trial until, finally on January 29, 1888, Alfonzo Poggi, of Bologna, replaced the head in a new acetabulum scooped out of the side of the ilium. Two years afterward the late Prof. Hoffa brought out his well-known method of detaching the muscles about the great trochanter and making a new acetabulum. In 1892 Lorenz modified Hoffa's procedure by making an incision from the anterior superior iliac spine downward and outward along the posterior edge of the tensor fascia femoris muscle. In 1895 Hoffa, having been convinced by Trendelenburg that loosening of the muscles attached to the greater trochanter was unnecessary, made an incision along the anterior edge of the greater trochanter

from its tip down. There have been practically no further developments of the open operative method since that date. While the bloody method was occupying the attention of the surgical world, Agostino Paci, of Pisa, was publishing his work by the bloodless method from 1888 to 1893. In 1894, at the International Congress in Rome, Lorenz and Hoffa came prepared to fight for their respective cutting operations, but Paci by this time had systematized his work. He gave his results on 23 cases of congenital luxations, besides 5 of pathological and old traumatic ones; also those of 10 other surgeons who had used his method; he submitted a specimen showing a perfect antemortem reposition; and finished by performing his bloodless method on a patient before the assembled surgeons. The effect might almost be described as ludicrous. No more was heard of cutting operations. Lorenz, in the following year, modified Paci's procedure and travelled far and wide exploiting it.

The majority of congenital luxations of the hip which one now sees can be replaced by the more or less modified bloodless method of Paci, but occasionally one sees a case which it is impossible so to reduce.

A person who has only one hip luxated, as in the third case, not infrequently has such an amount of disability as to demand relief. Should such a case not receive attention before say the age of ten or twelve years (it varies considerably), then the only other alternative is an open operation or they must bear their ills as best they can. If the case happens to be a luxation of both hips one will be apt to be much worse than the other. This was the condition in Case I. The right hip though luxated was still fairly fixed in its displaced position, the left, however, was so loose and caused such pain as absolutely to disable the patient and prevent her from earning her living. In the second case there was not only a luxation of both hips, but also the results of an infantile paralysis involving both lower extremities, as well as the muscles running from them to the trunk. Of course all the muscles were not paralyzed; some escaped, and by producing an artificial ankylosis in one foot (arthrodesis) and transplanting tendons in both feet the legs were made to acquire a certain degree of stability. The effect of the paralysis of the trunk muscles was partly counteracted by means of a firm corset. The left hip at first was luxated upward and anteriorly, the head being just below the anterior superior spine; later it has assumed a somewhat more posterior position. It was not, however, loose like the hip on the right side. The deplorable condition of this child with both hips luxated, together with the extensive paralyses, can be readily appreciated.

In 1897 I had operated on the left hip of this patient by Hoffa's original operation, but several years later it was found to have relapsed. In 1899 I showed before the Philadelphia Pediatric Society a child a little over five years of age, in which one hip had

been replaced by the bloodless and the other by the open operation, with success in each case.

In each of the 3 cases reported herewith the object was to fix the head of the femur in a new acetabulum so that in walking the weight

FIG. 1.—Gouge.

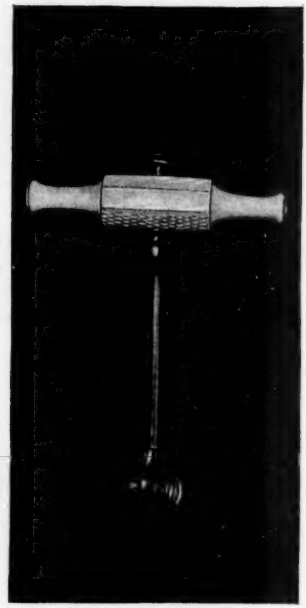

FIG. 2.—Burr.

FIG. 3.—The lever for lowering the head of the femur.

of the body would be borne by the bones and not by the soft parts, and this result was accomplished. In operating for this affection the incision I prefer is an anterior one straight down from the anterior superior spine. Hoffa's incision was along the anterior edge of the

greater trochanter, while that of Lorenz ran downward and backward from the anterior spine. The reason the extreme anterior incision is preferred is because of the better access which is obtained. The lateral incisions are difficult to separate in order to work properly. In the anterior incision, if more room is necessary, we can do as advised by Codivilla—separate the structures from the crest of the ilium from the spine back as far as desired. On the completion of the operation they are to be re-attached by means of sutures of chromic catgut.

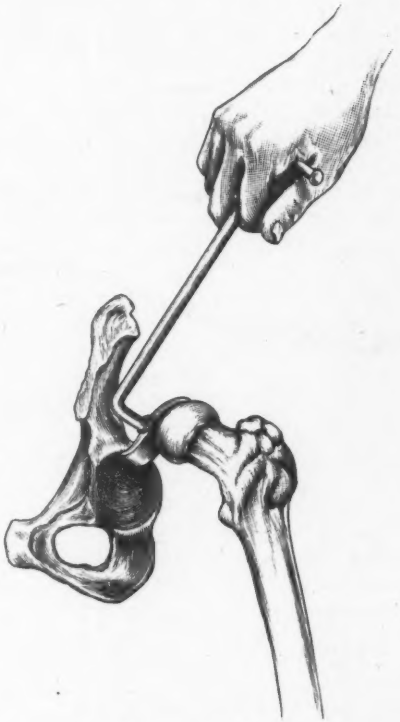

FIG. 4.—Method of replacing the head of the femur.

To deepen the acetabulum I prefer the gouge and burr devised several years ago.[1] The gouge (Fig. 1) has a round edge and is sharply bevelled on its outer side. It cuts quickly and efficiently and with it the chips are easily removed. The burr (Fig. 2) is one inch in diameter and has ten cutting teeth around one-half of its circumference only. The cutting side is used to smooth and deepen the

[1] Trans. Amer. Orthop. Assoc., 1899, p. 331.

new acetabulum at any desired spot, while the smooth side presents toward the femoral head, the cartilage covering which thereby remains uninjured. In order to facilitate lowering the head a lever (Fig. 3) was devised, consisting of a rod bent at a right angle and having a square handle at one end and a small curved plate at the other. By loosening the screws that hold the plate on, the latter can be removed and reversed for use on the opposite hip. The smaller plate is 4.5 cm. (one and three-quarter inches) long and is intended for children; the longer is 6 cm. (two and three-eighth inches) long and is intended for adults. A firm, square handle is essential to manipulate the instrument properly. In using it one end of the plate is hooked under the edge of the acetabulum, while the other end rests on top of the femoral head. By depressing the lever the head slides along the shallow groove of the plate into the acetabulum (Fig. 4). A. Codivilla, of Bologna, used a straight lever for this purpose.[2] A stout steel hook is also sometimes of service in lowering the head of the bone. In order to dilate and stretch the capsule and adjacent fibrous structures, the uterine dilator of Pryor (Fig. 5) has been found of service. It is very strongly constructed.

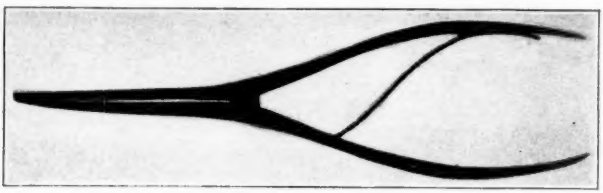

FIG. 5.—Uterine dilator of Pryor.

The incision used passes almost directly downward from the anterior superior spine of the ilium; this is between the anterior or inner edge of the tensor fasciæ femoris and sartorius muscles. I prefer this to the incision of Lorenz, which follows the posterior edge of the tensor fasciæ femoris and to that of Hoffa, who makes one along the anterior edge of the greater trochanter. One should avoid as far as possible injuring the branches of the deep circumflex artery and nerve as they cross the femur. Drainage may be used for twenty-four hours and the limb placed in a position of marked abduction in plaster-of-Paris. After eight weeks the plaster is to be removed, the limb brought down somewhat, and the patient allowed to go about on crutches.

Over two years have elapsed since the operation in the first case, and over a year in each of the other two cases, so that there is reason for hoping that the present results will be permanent. In order to avoid ankylosis it is in the highest degree desirable not to wound the cartilage on the head of the femur.

[2] Archives di ortopedia, 1902.

THE POSTOPERATIVE TREATMENT OF MALIGNANT DISEASE.

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The fundamental principles upon which is based the postoperative treatment of malignant disease with the *x*-rays are: (1) That some of the cells of the malignant growth have been left in the tissues; and (2) that the *x*-rays have a selective destructive action upon such malignant cells in their location in the tissues. If the first of these two conditions be absent, no *x*-ray treatment is indicated, and if the second principle be not well founded, the treatment would be useless. The discussion of this subject must, of necessity, therefore, resolve itself into a discussion of these two principles. In this discussion I shall take as a type carcinoma of the mammary gland, and when no other growth is mentioned this growth is assumed to be the one referred to.

That some malignant cells are usually left in the tissues after an operation for the removal of a malignant growth is amply proved by the experience of every surgeon in the recurrences that take place. A recurrence is an evidence that some cells were left. Without the existence and the proliferation of these malignant cells a recurrent growth could not appear. So common is the recurrence that in every text-book description of malignant growths there is mentioned the classical symptom, "a tendency to recur after removal." The difficulty in removing every cell is a natural consequence of the essential character of a malignant growth. Such a tumor grows peripherally and sends out offshoots, penetrating the surrounding tissues. The invading cells find ready and easy progress along the lymphatics. The gross mass of the tumor affords no true index to the limits of the cells that are leading the advance. Since there are no means of telling the confines of the malignant cells, it is but natural that some cells should be left when the main body of the tumor is extirpated.

The tendency of the cells to advance beyond the main mass is dependent upon the richness of the surrounding tissues in lymphatics, the proliferative activity of the tumor cells, and the manipulation of the tumor, before or during the operation, which tends to dislodge cells and assist their advance in the lymphatics.

A due appreciation of the anatomy and histology of the tumor and of the surrounding parts has recently led to a great improvement in the surgeon's operative technique, increasing the chances of removing all the malignant cells. Such, for example, is the operation to remove the adjoining axillary lymph nodes, then the lymphatic channels, and finally the tumor of the breast, endeavoring to get the whole out en masse, but beginning with the lymph nodes.

When malignant cells have been carried beyond the confines of

the nearest nodes and have invaded the circulation and been carried to distant parts, the possibilities of reaching them becomes correspondingly more difficult, because of the uncertainty of their existence and location.

The statistics of the surgeons each year show a steady diminution in the number of recurrences after operation. Twenty years ago practically every carcinoma of the breast that was removed was followed by recurrence or metastasis. Last year, at the meeting of the American Surgical Association in the symposium on "Carcinoma of the Breast," the recurrences reported varied from 23 per cent. to 80 per cent., the variation depending upon the operator, the operative technique, the stage of the growth when removed, and the length of time over which the observation extended.

After taking into consideration all these points regarding a thorough operation, the balance of the evidence is still strongly in favor of the probability that some malignant cells will be left in the tissues, from which a recurrence may arise. Since, then, it is necessary to destroy these remaining malignant cells to prevent a recurrence, and since the chances are that such cells do remain, it therefore becomes our duty to act upon the assumption that malignant cells are left in the tissues and to pursue that treatment which will completely eradicate them.

Our discussion now reverts to the question as to whether we have in the *x*-rays an agent that will accomplish this much-desired object. Even the most skeptical will acknowledge that the *x*-rays will heal superficial carcinomas. Many of us have seen them heal carcinomas more than an inch from the surface, and this without even producing a reddening of the overlying skin, thus giving evidence that the effect is a selective action upon the malignant cells. Microscopic study of such tissue will show granular disintegration of the actively proliferating cells of the carcinoma, while the protective resistant epithelial cells of the skin appear unaffected. A larger dose of the *x*-rays will finally produce in these latter resistant epithelial cells the same changes that are found to occur in the malignant cells with a smaller dose. The readiness and ease with which superficial carcinomas or epitheliomas heal without producing destruction or even redness of the surrounding tissues is evidence of selective action of the *x*-rays.

The question of recurrence after apparent healing with the *x*-rays rests upon the same principle as that of healing by any other procedure, namely, whether any malignant cells were left undestroyed. If the rays will destroy so many of the cells that there will be a disappearance of gross evidence of the growth, then by the continuation of the same destructive influence of the rays it is only reasonable to assume that all histological trace of the growth, or the last remaining malignant cell will finally disappear. When this is the case there cannot possibly be a recurrence. This is proved by

the fact that many cases so treated have not had a recurrence after many years, and consequently no malignant cells could have been left.

If the cells that are left were on the surface they would be readily destroyed, as we know to be the case with cells of all superficial carcinomas. Unfortunately the cells that may be left after an operation lie deeper in the tissues, and the difficulty in reaching them is in proportion to their depth. It could be argued that if the rays can be relied upon to destroy cells deep in the tissues, why should the rays not be relied upon to destroy the primary or original growth and so render surgical intervention unnecessary. The answer to this is in the fact that the cells of a primary growth are farther from the surface than are those cells that may be left after the tumor mass and other tissues have been removed. After such an operation no malignant cells are more than an inch and half from the surface unless they have invaded the intercostal spaces or deeper lymphatics. Unquestionably, the *x*-rays given in proper dosage can be relied upon to destroy malignant cells this distance from the surface. Many instances have occurred in which growths deeper than this have been made to disappear. The fact that *x*-rays can affect nodules this distance from the surface is well known by every Röntgen operator who has treated many recurrent growths of the breast. When such nodules disappear, it means that the malignant cells composing it have been destroyed and the detritus absorbed.

If some cells are destroyed, then why will not all be destroyed if within this distance and subjected to the same destructive influence? The answer is clearly that they will be. If, however, the distance is greater, or if the cells lie behind structures of greater density, such, for example, as the sternum or the ribs, the chances are that the malignant cells will not be destroyed. The following case is of interest: I treated a recurrent nodule over the sternum which was rapidly disappearing under *x*-ray influence, when symptoms of general carcinosis developed, and the patient died. The postmortem showed the practical disappearance of the nodule treated, but behind the sternum was a large carcinomatous mass which was unchecked and invading the lung. In addition to this mass there were metastatic growths in nearly every other internal organ. Such is the nature of a carcinoma. If the cells have wandered from the parent growth beyond the limits that are accessible to the *x*-rays, the postoperative treatment is useless, but if cells are left within this accessible zone they can be destroyed. Unfortunately we have no definite means of telling just after the operation whether or not cells have already wandered beyond this accessible zone through the intercostal spaces or to distant parts.

For this reason all prognosis must be guarded. In a large proportion of cases we know from experience that remaining malignant

cells are likely to be only in this accessible zone. It, therefore, is clearly our duty, if we would give the patient the greatest chance for complete eradication of the malignant growth, to give post-operative *x*-ray treatment.

As to the action of the *x*-rays in blocking the lymphatic circulation by producing proliferation of the endothelial cells and by the formation of fibrous tissue with its consequent contraction, this is a possibility stated by some observers, but the more rational basis seems to me to be the proved direct selective action of the rays upon the malignant cells.

In regard to the practical application of the *x*-rays in postoperative treatment, my own method is based upon the assumption that there are scattered through the area accessible to the destructive influence of the rays very small masses of malignant cells. By experience we know that small recurrent nodules can be made to disappear in two or three series of exposures, each series having about five exposures, and each exposure being of ten to fifteen minutes duration at ten inch distance, the milliamperage in the secondary being $\frac{3}{4}$ to 1, and the penetration of the tube necessary according to the Benoist scale 4 to 5. The exposures in a series are given daily. A series is about sufficient to produce an erythema. A week to two weeks elapse between series, in order to give time for the erythema to develop and fade. Two series will be usually sufficient. In far advanced cases it is probably safer to give three or more series, as the remaining cells may be more numerous and deeper in the tissues. The *x*-ray treatment should be begun about five days after the operation. I think it better to wait until primary union has a good start before applying the rays, because the rays may retard the union, as it undoubtedly has a decidedly destructive influence upon all actively proliferating cells. The granulation tissue or the reparative tissue that brings about primary union comes under the rule concerning the selective action of the rays, which rule is that the rays affect a tissue in proportion to the density of cells and in proportion to the proliferation or functional activity of such cells. For this reason union should have at least five days start before applying the rays.

The reason against an exposure two or three times a week for several weeks or months is that such small dosage is not sufficient to destroy the cells. It simply may retard their development so long as the treatment is kept up. If cells are to be destroyed, a certain dosage must be given in such short time that the influence will be cumulative and the total cumulative dose sufficient to produce a destructive effect. I have found such procedure satisfactory in treating superficial carcinomas and known recurrent malignant nodules. Too great stress cannot be laid upon the necessity of every *x*-ray operator knowing his apparatus so that he can foretell the results of different dosage.

In conclusion, I may say that postoperative *x*-ray treatment of malignant disease is indicated because in every attempt to remove surgically a malignant growth the chances are that cells of the growth have been left in the tissues, and also because we have in the *x*-rays an agent that in a large proportion of the cases will completely destroy these cells. It, therefore, becomes our duty to give the patient the increased chances of a permanent cure.

THE DIFFERENTIATION OF COMMON TYPES OF PROTRACTED FEVER.

By David Bovaird, Jr., M.D.,

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The anxiety aroused by the presence in a patient of a continued fever for which we can find no adequate cause is well known. Of recent years a number of interesting and instructive cases of this character have come under observation in the Presbyterian Hospital, and a review of them may prove of value. We may classify these cases under the following heads: (1) Typhoid fever, (2) tuberculosis, (3) septicemia, (4) influenza, and (5) unexplained fever. The absence of malaria from this list may be thought remarkable, but it is now established beyond question that in this latitude malaria can easily be recognized by the examination of the blood and the use of quinine. A fever which shows no parasites in the blood and does not yield to quinine is not malaria. We have therefore no longer any difficulty from that source.

1. Typhoid Fever. Protracted cases of typhoid fever are not uncommon. McCrea gives the average duration of the primary attack as twenty-nine days, but it may well be prolonged to forty or fifty days. We have in our records one case of sixty days, and longer cases are reported. Such prolongation of the fever always gives rise to anxiety, although, as a rule, if the fever is the chief consideration we may be confident of a favorable outcome. The greatest cause of anxiety in these cases is usually that of diagnosis. As the fever is protracted beyond its usual limits we begin to question whether the diagnosis is certain, whether we may not be dealing with some other disease, such as tuberculosis or septicemia. In the days when we were forced to rely wholly upon bedside observation this uncertainty often gave rise to great anxiety. The aids brought to our assistance by the clinical laboratory have naturally lessened our difficulties. By means of the diazo reaction, the leukocyte count, the Widal reaction, and blood cultures, the diagnosis of typhoid fever can now

be established with such certainty that there is rarely ground for doubt. We sometimes fall into error by persisting in regarding a case as typhoid fever despite the negative evidence of these various tests. If in any case believed to be typhoid fever we have not by the end of the third week obtained satisfactory evidence, from clinical observations and laboratory tests, of the correctness of that diagnosis, we had best seriously review it.

The question naturally arises, What is satisfactory evidence of typhoid fever in the cases of protracted fever of which we are speaking? The enlargement of the spleen so often made much of belongs also to the diseases with which typhoid fever is most likely to be confused—tuberculosis and septicemia. It is perhaps more frequent in typhoid than in either of the other fevers, but not sufficiently so to render its presence of definite value. We may say the same of the abdominal symptoms—distention, tympanites, diarrhœa. In short, on the clinical side the symptom of most help is the typhoid roseola. In the Johns Hopkins cases of typhoid the eruption was found in 93 per cent. of the white patients, in 55 per cent. of the black. Taken in conjunction with other symptoms suggestive of typhoid it may be safely accepted as determining the diagnosis. The characteristic rash consists of small, round, discrete, rose-colored spots, varying from 2 to 4 mm. in diameter, disappearing on pressure either flat or sufficiently raised to be definitely felt above the surface, developing in successive crops on the abdomen, chest, or back. They usually appear during the second week, but it is to be remembered that they may not appear until much later—in some cases not until the fever has subsided. The bright color of the spots seen on their appearance fades gradually in three to five days, leaving possibly a slight brownish pigmentation. The typhoid spots never become vesicles or pustules and are never acuminate. They are therefore easily distinguished, as a rule, from chance eruptions of acne, miliaria, and the like. No such spots are seen in the other fevers here under consideration. The only prolonged fever in which spots not easily distinguished from those of typhoid fever do occur is trichinosis, but this affection is readily recognized by other features, especially the œdema of the face, pains, leukocytosis, and eosinophilia.

Of the laboratory tests, the diazo reaction is of slight value. It is more frequent in typhoid than in other fevers, but not sufficiently so to render its presence more than suggestive. A persistently low leukocyte count, with or without a relative lymphocytosis, belongs to typhoid fever and tuberculosis. The Widal reaction, if obtained repeatedly by a qualified observer, ought to be pathognomonic. Its continued presence in a doubtful case is regularly decisive. While we know that the reaction may be absent in some cases, we also know that it is found at some period of the fever in 95 per cent. of the cases in which it is carefully sought. Its value in a case of doubtful protracted fever is therefore great.

The demonstration of typhoid bacilli in the blood is, of course, conclusive. Equal importance attaches to the demonstration of the bacilli in the urine or cerebrospinal fluid, or even in the feces. The cultivation of the bacilli from any of these sources is, however, attended with considerable practical difficulty. When one has access to a first-class laboratory and an experienced bacteriologist, these procedures may clear up a case which would otherwise remain a puzzle.

The following case well illustrates the difficulties of diagnosis even when every resource at our command is employed, and the value of the Widal reaction and blood cultures when positive results are obtained:

CASE I.—M. B., aged forty-six years; a housewife. She had had a chronic endocarditis for some years, and was treated in the Presbyterian Hospital from April 3 to May 12, 1907, for lobar pneumonia and chronic endocarditis. She was readmitted on September 27 on account of an increase in her symptoms of cardiac failure. Under treatment her condition improved. The temperature was practically normal until October 20, when she had a chill and a sudden rise to 104°. At this time the pulse, previously ranging from 60 to 80, rose to 96 to 108, and her dyspnœa was somewhat increased. Nothing in the physical examination at this time explained the chill and fever. For two days following the chill the temperature was moderately high, 101° to 103°, then it rose again, and remained from 102° to 105° for many weeks. The pulse remained rather slow in proportion to the fever. The spleen became enlarged so that it was easily palpable. The abdomen was distended and tympanitic. The bowels were constipated. At times the patient's mind was rather dull, but not remarkably so. She sweated profusely. The diagnosis lay between typhoid fever (acquired in the ward) and an added infection of the endocardium (malignant endocarditis). For five weeks there was no material change in the conditions. During this period the urine regularly gave the diazo reaction of Ehrlich; the leukocyte count ranged from 10,000 to 12,000, but on one occasion sank to 6000. Repeatedly trials of the Widal reaction resulted negatively, and two blood cultures gave no growth. Neither the characteristic roseola of typhoid nor the petechial rash of malignant endocarditis appeared. On the whole, the clinical course seemed to favor the diagnosis of typhoid fever, but the rarity of typhoid infections in the hospital and the absence of conclusive evidences of typhoid kept us in doubt. On the other hand, the suddenness of the onset and a certain intensification of the signs of the chronic endocarditis strongly suggested the possibility of malignant endocarditis, and none of the findings were conclusively against that diagnosis. On the thirty-seventh day of the fever the Widal reaction was obtained, and this finding was confirmed three days later, while a blood culture taken on the thirty-sixth day gave a

growth of the typhoid bacillus. The patient finally succumbed in the ninth week of the fever, and the autopsy confirmed the diagnosis thus tardily established.

The further consideration of the differential diagnosis will be taken up in connection with the discussion of the types of protracted fever.

2. TUBERCULOSIS. The tuberculosis which belongs to our subject is the acute miliary form, of which there are two fairly distinct types: (1) The typhoid, and (2) the pulmonary. A summary of two cases illustrating these types follows:

CASE II.—H. G., aged twenty-seven years; admitted June 23, 1904; died August 3, 1904.

History. Family: Negative. Personal: Negative. Previous: Pleurisy five years ago for one week. Gonorrhœa one and one-half years ago. Present: For two weeks easily tired and lacking in energy; nine days in bed on account of headache, backache, and fever. He has felt better, but remained in bed on orders. On admission, temperature, 104°; pulse, 72; respirations, 20. Physical examination at this time entirely negative.

Course. Continued fever, from normal to 105°, eight weeks in all. Usually from 100° to 102° to 103°. Pulse from 72 to 100, more rapid and feeble at end. Respirations, 20 to 28. Loss of flesh and strength, exhaustion, moderate anemia.

Physical Signs. Spleen became palpable. No distention or tenderness of abdomen. No eruption. Signs of a slight general bronchitis.

Laboratory Tests. No Widal; no diazo; blood cultures negative. Cultures from feces, no typhoid. Sputum always negative, rarely obtained. Urine negative.

BLOOD EXAMINATIONS.

	June 23	June 29	July 6	July 7	July 17	July 19	July 22	July 26
Hemoglobin	.....	.....	.....	50.0%				
Red cells	.....	.....	.....	4,136,000				
Index	.....	.....	.....	0.61				
Leukocytes	6000	5200	4000	5000	4300	3800	7300	4300
Polynuclears	.....	.....	.....	80.0%	.....	.....	.....	97.0%
Large mononuclears	.....	.....	.....	1.0%				
Small mononuclears	.....	.....	.....	18.0%	.....	.....	.....	3.0%
Eosinophiles	.....	.....	.....	1.0%				

Autopsy. Acute general miliary tuberculosis.

It is to be noted that in this case we found the leukopenia regarded as characteristic, but the differential counts showed in one instance

a definite increase of the polynuclear leukocytes, and in the other an overwhelming predominance of these cells.

CASE III—L. S., aged twenty years; admitted April 3, died June 24, 1906.

History. Family: Good. Personal: British Guiana until six months ago, when she came to New York; otherwise negative. Previous: Measles, whooping-cough, dysentery in childhood; dyspepsia for six months. Present: For one week not well, "caught cold," tired and easily fatigued; two days ago a chill, headache, and fever; the same afternoon a second chill; in bed since onset; complains only of fever, headache, prostration, anorexia, and constipation. On admission, temperature, 102°; pulse, 102; respirations, 20.

Course. Continuous fever, 100°, 102°, and 103°, rather irregular in type. Fever in all lasted three months. Pulse rather rapid, 80 to 100 to 120. Respirations, 20 to 30; in last weeks 30 to 40. Gradual loss of flesh and strength and increasing anemia. Always comfortable and cheerful.

Physical Examination. Entirely negative at beginning, except palpable spleen. April 30, by Dr. Baldwin, of Saranac, no pulmonary lesion. June 14, signs of a general bronchitis.

Ophthalmoscopic examination by Dr. Parker: one small area in right eye suggestive of miliary tubercle.

In final weeks occasional cyanosis of fingers and lips, gradually deepening and becoming continuous.

Laboratory Tests. Widal always negative; blood cultures negative; feces cultures negative. No malarial organisms in blood. Urine: 1015 to 1025, albumin, faint trace, rarely casts, no pus. Diazo reaction repeatedly positive.

BLOOD EXAMINATIONS.

	Hemoglobin. Per cent.	Red cells.	Index. Per cent.	White cells.	Polynuclears. Per cent.	Transitionals. Per cent.	Large mononuclears. Per cent.	Small mononuclears. Per cent.	Basophiles. Per cent.	Eosinophiles. Per cent.
April 3 . .	78	6,024,000	0.68	8,100	82.0	0.5	2.0	15.5		
April 4 . .	...	.....	.....	9,600	64.0	5.5	0.5	23.5	.....	6.5
April 7 . .	...	.....	.....	.....	82.0	.....	10.4	6.0	0.4	1.2
April 24 . .	76	.....	.....	13,800	84.5	1.0	3.0	10.5	0.5	0.5
May 6 . .	77	.....	.....	16,100						
May 8 . .	...	.....	.....	16,300						
May 10 . .	...	.....	.....	.. ...	72.0	3.0	8.0	14.0	.....	2.5
May 12 . .	...	.....	.....	.....	74.5	1.5	11.5	16.5	.....	2.5
May 22 . .	...	.....	.....	10,500	82.0	4.0	2.0	7.0	.....	5.0
June 8 . .	69	4,704,000	0.73							
June 22 . .	...	.....	.....	19,000						

Autopsy. Acute general miliary tuberculosis, the lungs crowded full of miliary tubercles.

Special attention is called to the variability of the leukocyte count, both absolute and differential. Out of seven counts, only one, that of April 4, gave what is commonly stated to be the characteristic blood picture of acute miliary tuberculosis, an absence of leukocytosis, with an increase in the proportion of lymphocytes. The rapid variation of the differential counts indicates the need of great caution in interpreting the meaning of any one of them. The most careful examination of the lungs as late as April 30, more than a month after the onset, gave no signs, although at that time there must have been large numbers of miliary tubercles in the lungs.

The resemblance of the first type of acute miliary tuberculosis to typhoid fever is so close that for weeks a differential diagnosis is usually impossible. They have in common the fever, prostration, gradual emaciation, and slowly increasing anemia. Each shows an absence of leukocytosis, or leucopenia, with usually an increase in the percentage of lymphocytes. Either may give the diazo reaction. Either may show moderate enlargement of the spleen. Either may have tympanites and diarrhœa. Miliary tuberculosis with intestinal lesions (ulcers) may even show blood in the stools. Either may give a Widal reaction. The resemblance is so close that in some cases a decision between them must be left to the autopsy.

In most cases, however, we can by care anticipate the conclusion. Acute miliary tuberculosis of this type looks like mild typhoid fever, but it may be distinguished by these points:

1. A previous tuberculosis of any part of the body.

2. The fever of miliary tuberculosis is more irregular than that of typhoid. It shows a greater daily variation: it may be low all of one day, to rise again the next; it more frequently shows sudden brief drops to normal or below with quick recovery.

3. When a typhoid fever of similar severity would be improving, the patient with miliary tuberculosis is stationary or still failing. Thus, at the end of the third or fourth week the temperature, instead of falling, continues or runs a higher course.

4. Hemorrhage from the bowels in any degree, although it may occur, is most uncommon in tuberculosis.

5. Of the decisive features of typhoid fever mentioned above, the roseola, the typhoid bacillus in the blood or excreta are absent.

6. The possibility of the occurrence of a Widal reaction in tuberculosis, especially the acute miliary form, must be admitted. The reaction in these cases, while not altogether typical, so closely resembles that obtained in typhoid that even the most skilled observers find difficulty in distinguishing them, and the inexperienced may see no difference. It still remains true that the repeated finding of the Widal reaction is more characteristic of typhoid than of tuberculosis.[1]

[1] Wood, Chemical and Microscopic Diagnosis, p. 236

The second (pulmonary) type of acute miliary tuberculosis is much like the preceding, and presents the same difficulty of diagnosis for weeks. The careful observation will regularly disclose some important points:

1. Attacks or periods of cyanosis of the lips (and other mucous membranes) and the finger tips. This cyanosis is at first slight and variable, quite definite at one time, then disappearing entirely for a time. It is not caused by any ascertainable disturbance of the circulation; the pulse remains the same. It is free from any distress on the part of the patient—in fact, the comfort of the patient, despite the definite cyanosis, is quite notable.

2. The signs of diffuse bronchitis, which belong to typhoid fever and tuberculosis in the early stages, instead of gradually clearing up as they should in typhoid, gradually increase. The expansion of the chest and its resonance are slowly and insidiously impaired, yet without definite areas of consolidation. It is often amazing at autopsy to find a lung packed with miliary tubercles, which have given no pronounced signs during life.

3. The periods of cyanosis become more frequent and longer until the symptom becomes continuous. The respiration quickens gradually, but to the end there is no real dyspnœa or distress.

4. The cough is always much less than the signs would lend us to expect, and may be absent even to the end. Similarly, expectoration most often is lacking, and even when present does not show bacilli.

In connection with this question of the diagnosis of tuberculosis mention may here be made of the test reactions of von Pirquet and Calmette. For some reason not yet satisfactorily explained both these reactions fail in acute miliary tuberculosis, so that they are not of value in the cases we are at present discussing.

3. Cryptogenic Septicemia. The third common cause of protracted fever, and in our experience much the most frequent one, is cryptogenic septicemia. When we have to do with fever in association with suppurating wounds, an infected uterus, large abscesses, etc., the explanation of the fever is, of course, easy. In the group of cases to be here considered, however, the origin of the septicemia is not revealed and the search for it is often futile.

The cases which belong in this group may be readily classified. (1) Blood infections; malignant endocarditis; pyogenic organisms found in blood. (2) Local infections; latent; no organisms in blood; symptoms produced by absorption of toxins from some hidden focus of suppuration, which finally develops into a localized abscess, such as abscess of the liver, perinephritic abscess, or empyema.

The following abstracts of cases illustrate these different types:

Case IV.—*Malignant Endocarditis.* F. M., aged eleven years; admitted September 25, 1907; died October 1, 1907.

Previous history of chorea and rheumatism, pneumonia, and measles. Present history: For ten days before admission she had

had fever and headache and had occasionally been delirious. On her admission her temperature was 103.8°; pulse, 120; respirations, 48.

The physical examination at this time showed marked apathy and prostration, a coated tongue, an enlarged heart with systolic murmurs at the base and apex, a rapid pulse, but of good quantity, the abdomen distended and tympanitic, and an enlarged and palpable spleen.

The leukocytes on admission were 15,200. The clinical diagnosis at this time was typhoid fever. During the following six days the temperature was continuously high, ranging from 102° to 105°, the curve being altogether like that of most severe typhoid fever. The pulse grew steadily more rapid and weaker and the apathy and prostration deepened. In a general way the course was that of severe typhoid. But on the 29th, four days after admission, the leukocytes were found to number 31,500 and a differential count showed 87 per cent. polynuclears, 1 per cent. transitionals, and the mononuclears, large and small, only 12 per cent. On the same night a number of petechial spots appeared on the chest and side of the neck. Later, paralysis of the right side developed. The cardiac signs became more pronounced. Finally, a blood culture taken three days after admission showed abundant growths of staphylococci.

The rise in the leukocyte count on the 29th showed that the case was not uncomplicated typhoid fever, while the rapid evolution of the petechial eruption and subsequent paralysis indicated clearly a malignant endocarditis. The result of the bood culture confirmed this diagnosis.

Case V.—S. M., aged nineteen years; factory hand; admitted November 9, 1905; died June 21, 1906.

History. Family: Negative. Previous: Heavy lifting in room at high temperature. Malaria two years ago. Present: For four months feeling poorly. Hands and feet cold and chilly sensations at times. He had no dyspnœa, œdema, or shortness of breath. Bowels constipated. No nausea or vomiting. As he did not improve, he went to a physician, who told him he had heart trouble and that he had better stop work and take a rest. Since then he has been getting up late in the morning, and has rested much during the day, but without benefit. His chilly feelings continue. He has palpitation when he attempts to get about, and is occasionally dizzy. No dyspnœa; marked anorexia, but no nausea or vomiting. No nose bleed or headache. Stools normal. All this time he has had fever and sweated a good deal at nights.

Physical Examination. Heart: Apex impulse maximum in fourth space two and three-quarter inches to left of midline, and in fifth space three inches to left of midline. Left limit of dulness corresponds. No enlargement made out. Action regular, forcible, not rapid. At the apex there is a soft blowing systolic murmur transmitted to the axilla and heard behind, and also over whole pre-

cordium, being more accentuated over the pulmonic area. Basal sounds are clear, the second pulmonic being the louder.

Pulse regular, a little rapid, good force and size, soft, wall palpable, markedly dicrotic, marked pulsation of arteries in neck. Examination otherwise negative.

Course. During the seven months of his stay in the hospital this patient had more or less daily fever. At times the fever would be slight, but usually the temperature at some time of the day would reach 101° to 103° or 104°. During the early weeks the fever was continuous; later it become irregular and much of the time intermittent in type. The more important features of the daily notes are given below. The condition of the heart remained throughout practically the same. The patient's friends finally insisted upon removing him from the hospital, and the later history is not known.

BLOOD EXAMINATIONS.

	Hemoglobin. Per cent.	Red cells.	Leukocytes.	Polynuclears. Per cent.	Large mononuclears. Per cent.	Small mononuclears. Per cent.	Transitionals. Per cent.	Eosinophiles. Per cent.	Basophiles. Per cent.
November 9	55	3,200,000	6,200						
November 10	...	.....	12,000						
November 20	...	.....	8,700						
November 28	...	.....	10,000						
December 22	72	3,840,000	19,000	76.0	7.5	12.5	2.5	1.5	
December 29	...	.....	12,100						
January 2	50	3,272,000	13,200	76.0	7.0	14.0	2.5	0.5	
January 9	...	.....	8,100	84.5	2.5	11.0	1.5	0.5	
January 15	...	.....	.....	77.5	4.0	14.5	3.0	1.0	
January 24	...	.....	10,300						
February 12	...	.....	16,100	76.5	2.0	11.0	5.0	0.5	
March 6	...	.....	14,300						
March 30	...	.....	19,600	90.0	0.5	6.5	2.5	0.5	
April 16	...	.....	8,800	71.0	0.5	19.5	7.0	1.5	0.5
April 24	...	.....	22,400						
May 22	...	.....	9,400						
June 16	...	.....	11,800	89.0	0.5	5.0	5.5		

November 25, a systolic thrill at apex. November 29, spleen palpable. December 1, pain in left hypochondrium; spleen large. December 15, a few petechial spots on abdomen. January 1, murmurs same. January 2, a few new petechial spots. January 15, more petechiæ on chest and back. January 22, severe abdominal pain; heart same. January 26, pain in left shoulder. February 14,

from time to time new petechiæ appear. March 1, red blood cells in urine and tenderness over left kidney. March 14, temperature normal for several days. March 30, temperature not above 100° for two weeks. April 9, temperature not above 100° for two weeks. May 16, temperature shows occasional shoots to 102°. June 7, fever irregular; some burning pain on micturition and blood in urine.

A blood culture on November 28 was negative; a second, on December 22, yielded a pure growth of Staphylococcus pyogenes aureus.

Urine, 30 to 70 ounces; average, 50 ounces; specific gravity, 1015 to 1020; albumin, trace, to 24 to 31 per cent.; hyaline and granular casts; rarely blood and blood casts.

Comparison of the results of the blood counts, especially the absolute and differential leukocyte counts, with those of the second case of acute miliary tuberculosis shows that the only notable difference lies in the more marked reduction of hemoglobin in the latter case. The leukocyte counts show closely similar variations both in totals and in the distribution of the several types.

CASE VI.—*Perinephritic Abscess.* J. M., aged twenty-three years; iron worker; admitted June 3, 1907; transferred June 18, 1907.

History. Family, previous, and personal irrelevant. Present: For three months complaining of bloating and pain in the abdomen, the latter not related to taking of food. For three weeks more or less vomiting of mucus. At one time he vomited a small quantity of blood. He has some pain low in the left side on deep breathing. On admission, temperature, 101.2°; pulse, 92; respirations, 21.

Physical examination at this time elicited nothing of importance. The patient looked as though uncomfortable, but was thought to be exaggerating his sufferings.

Course. Fever continuous, 100° to 104°; daily variation, 2° to 3°; duration in all about one month. Pulse, 72 to 96; respirations, 20 to 24.

BLOOD EXAMINATIONS.

	Hemoglobin. Per cent.	Red cells.	Leukocytes.	Index. Per cent.	Polynucleears. Per cent.	Large mononucleears. Per cent.	Small mononucleears. Per cent.	Eosinophiles. Per cent.
January 4 . . .	...	.....	14,200					
January 5 . . .	80	4,200,000	10,000	1	77	7	15	1
January 8 . . .	...	.....	10,600					
January 9 . . .	...	.....	12,900					
January 12 . . .	...	.....	17,100					
January 13 . . .	...	.....	16,100					
January 16 . . .	...	.....	23,100					

At the end of two weeks patient developed some swelling and tenderness in the iliolumbar region. He was transferred to the surgical side, and a perinephritic abscess of some size was evacuated. Growth from abscess showed Micrococcus pyogenes aureus. Recovered promptly. Not until the development of the local signs was it possible to make the diagnosis.

Attention is called especially to the low total leukocyte counts in the first week and the normal differential count.

CASE VII.—*Abscess of the Liver.* F. S., aged thirty-five years; admitted May 6, 1904; transferred June 13, 1904.

History. Family and previous personal history of no help. Present: Began twelve days before admission with headache, malaise, and pain in the bones. Fever constant from 101° to 103°. For one week some pain on right side on deep inspiration. On admission, temperature, 100°; pulse, 96; respirations, 24. Physical examination at this time entirely negative.

Course. A continuous fever ranging from 100° to 105°; daily variation of from 2° to 3°; lasting about seven weeks before its origin was made out. Pulse, 80 to 100; respirations, 20 to 24.

BLOOD EXAMINATIONS.

	Leukocytes.	Polynuclears. Per cent.	Large mononuclears. Per cent.	Small mononuclears. Per cent.	Basophiles. Per cent.	Eosinophiles. Per cent.	Lymphocytes. Per cent.
May 6	19,300						
May 9	18,800						
May 15	17,500						
May 18	10,400						
May 19	12,200	72.4	7.6	18.8	0.4	0.8	
May 22	15,200						
May 23	16,500						
May 25	14,200						
May 27	.....	73.0	8.0	.....	.....	1.0	1.8
May 28	14,800						
May 30	13,600						
June 3	14,200						
June 5	14,000						

Blood culture, May 27, negative,

Urine, sputum, and feces frequently examined without result. Gradually increasing resistance in right upper quadrant of abdomen and some slight tenderness there. Patient became weaker

and more anemic; was transferred to the surgical division, and operation disclosed an abscess of the liver.

In this case we note that after three fairly high counts the leukcytes sank to a rather indeterminate level and that both differential counts were normal.

CASE VIII.—*Subphrenic or Retrohepatic Abscess.* J. L., aged eighteen years; oiler; admitted November 23, 1904; transferred December 22, 1904.

History. Family and previous history of no aid. Present: He has had a cold and cough for some time. Three months ago he stopped work on account of abdominal pains, general in distribution, but most marked in umbilical region. Sometimes these pains shifted to the right side of the abdomen, especially if he slept on that side. The pains were most likely to come on after meals and were accompanied by bloating, but they also came when he was at work and interfered with his work. His appetite has been normal, his bowels very constipated. During his three months' illness he has lost twenty pounds in weight and much strength. For at least three weeks of this time he has wakened nearly every night with fever and chilly sensations. At one time his temperature reached 104° according to his physician. The pain in abdomen radiates at times to chest and shoulder (right). On admission, temperature, 99.8°; pulse, 92; respirations, 24. Physical examination at this time showed only a marked anemia; no cause for fever.

Course. Intermittent fever, from 97° to 104.8°, with frequent chills, lasting at least seven weeks before origin was found. Pulse rapid with chills, but usually 80 to 90; respirations, 20 to 30.

BLOOD EXAMINATIONS.

	Hemoglobin. Per cent.	Red cells.	Leukocytes.	Polynuclears. Per cent.	Large mononuclears. Per cent.	Lymphocytes. Per cent.	Basophiles. Per cent.
November 24	90	....	13,400				
November 25	...	.....	13,300				
November 28	70	3,904,000	11,000				
December 2	...	....	10,600	64	10	26	
December 5	...	.....	18,000				
December 6	...	....	16,000	72	9	18	1
December 8	...	.....	14,300				
December 10	...	.....	14,600				
December 14	...	.....	16,500				
December 16	...	.....	9,100				
December 17	...	.....	9,600				

The patient gradually became weaker and more anemic. To careful observation there seemed some slight enlargement of the right side in region of liver. There was occasionally a moderate epigastric tenderness, but the signs were so slight and variable that it seemed not wise to attach too great weight to them.

At one time, on account of cough, expectoration of mucus, and a few localized rales, it was thought that he must have pulmonary tuberculosis. We were, however, finally convinced that the trouble lay in the region of the liver. He was transferred and operated upon, an abscess being found posterior to and involving the right lobe of the liver. The patient finally died of exhaustion resulting from profuse hemorrhage from the liver wounds. Cultures from abscess yielded Staphylococcus pyogenes albus.

Again we see that in the case of a suppurative inflammation the leukocyte count only once in eleven times rose to a level regarded as suggestive of pus. One of the two differential counts suggested tuberculosis, the other was normal. In the early weeks of observation in the hospital tuberculosis seemed the most probable diagnosis. The gradual enlargement of the right side of the thorax, the marked anemia, rather frequent chills, and sweating ultimately led to a correct diagnosis.

Case IX.—*Empyema.* F. D., aged four years; admitted October 25, 1907.

History. Family: Negative. Previous: Pneumonia two years ago and in January, 1907. Dry cough since. Attack of pain in right lower quadrant abdomen lasting one week in May, 1907. Present: Fever and pain in abdomen since October 6. Occasional vomiting and cough. Pain agonizing at times. Chills repeated. On admission, temperature, 103°; pulse, 144; respirations, 40.

Examination. Anemia; emaciation; tenderness right side abdomen; bulging of right lower thorax.

Course. Fever 98° to 104°; very irregular, lasting in all over a month before the cause was found; cough; vomiting; abdominal pain.

Blood Examinations.

	Hemoglobin. Per cent.	Leukocytes.
October 25	65	40,000
October 26	...	31,000
October 31	...	14,500
November 8	...	22,700

Urine, normal; sputum, no tubercle bacilli; no reaction to ophthalmotuberculin test. Operation November 9; localized collection of pus in right pleura; pleural culture, pneumococcus.

This case is reported with interest, for here the height of the leukocyte count and the course of the fever taken with the scant indication of an apparent enlargement of the right side of the thorax

led to the suggestion that the boy had an empyema some time before physical signs justifying that diagnosis could be had.

Holt[2] reports a case of high temperature for three months in a boy two and one-half years of age, in whom the most careful study failed to disclose the cause of the fever. Briefly, the symptoms were fever, varying from normal to 106.2°, a little cough, slight acceleration of respiration, progressive emaciation and exhaustion, with varying signs over the lungs, never sufficient to justify the introduction of an exploring needle. At the autopsy, which was made by me, we found two small sacculated empyemas, one on the right side situated on the diaphragmatic surface of the lung near its anterior border, the other on the left side at the base of the lung and close to the spine. During the course of the fever the patient showed a leukocytosis varying from 10,500 to 28,000.

Delafield reports a similar case, the patient being a woman, whose fever lasted 234 days in all, and the empyema was found only at autopsy.

One should not leave the subject of protracted fever in children without remarking that in some instances the explanation is to be found in a suppurative pyelitis, the origin of which it may be quite impossible to explain. Difficulty in these cases arises only from failure to examine the urine. In young children especially, on acount of the difficulty of obtaining the urine, the examination is likely to be omitted. I have seen one case in a child two years of age in which fever ranging from 102° to 106° and persisting for three weeks was twice attributed by a distinguished consultant to a pneumonia which failed to appear. The examination of the urine at once showed an active pyelitis, and appropriate treatment promptly put an end to the fever. Instances of such cases running months before detection are on record.

Differential Diagnosis. *Malignant Endocarditis.* In its typical form malignant endocarditis is easily recognized. The cardiac disturbance, with presence of murmurs, the characteristic petechial rash, and the symptoms produced by the lodgement of emboli in various parts of the body make a clinical picture easily interpreted. In some cases, however, the cardiac symptoms are so slight as to be easily overlooked or undervalued, the rash and the embolic phenomena are absent for long periods of time, and the patient shows only an irregular fever, accompanied by increasing anemia and prostration. If limited to the interpretation of the clinical symptoms, we may well find it impossible to reach a definite diagnosis in such cases. But blood cultures will, as a rule, promptly clear up the mystery. A simple culture may fail, but a second or third will almost surely detect the offending organism.

Of recent years we have had an unusual number of cases of malignant endocarditis in the wards of the Presbyterian Hospital, and the

[2] Archives of Pediatrics, January, 1902, p. 22.

blood cultures have been regularly successful. With relation to the cases here reported, attention is called to the following points:

1. The absence of an indication, either in the history or in the body of the patient, of the source of infection.

2. The very irregular type of fever and the long periods of comparative freedom from fever.

3. The marked anemia, progressive and accompanied by progressive emaciation.

4. The low leukocyte counts, although the blood may contain many pyogenic organisms.

5. The typical petechial eruption is of the greatest value in diagnosis. This eruption will often be found in the palpebral conjunctiva (lower lid); in some instances when it cannot be found elsewhere (Janeway).

6. The chronicity of the disease, six to nine months in some cases.

Localized Abscesses or Suppurations. In these cases the chief symptoms are those found also in malignant endocarditis: (1) Fever, very irregular in type; sometimes repeated chills and sweating. (2) Progressive anemia and emaciation. (3) Absence of any indication of the source of infection for weeks or months.

Blood cultures are, however, negative, and we may for long periods be quite unable to reach a satisfactory diagnosis, until at length the characteristic signs of a local suppuration or abscess develop. The duration of this period in these cases is quite striking. The empyema patient was under observation for a month, the perinephritic abscess gave a history of three and one half months, the retrohepatic abscess of four months. Holt's patient was under observation for three months, and then the local collections of pus were found at autopsy. In Delafield's case 234 days of fever were recorded and again the explanation was found only at the autopsy.

The diagnosis presents the very greatest difficulties. Unless we may rely upon von Pirquet's cutaneous- or Calmette's ophthalmic-tuberculin test, we have at present no reliable means of differentiating these cases from those of miliary tuberculosis. In one of the series quoted the leukocyte count was high enough (40,000, 31,000, and 23,000) to point clearly to a suppurative process, but in none of the others were the counts of definite value. The differential counts upon which so much emphasis has of late been laid as a symptom of pus in certain localities are so variable that it is quite impossible to interpret them. We must in these cases rely upon unremitting vigilance for the detection of the signs of a definite abscess or suppuration.

4. Influenza. From time to time during the season when influenza is prevalent in the city we see cases of continued fever in which the best explanation of the fever is the presence of an influenzal infection without local lesion. The following cases illustrate this type of fever fairly well, though both are relatively

brief. In private practice it is not very unusual to meet such cases running for a month or more:

CASE X.—Miss S., aged thirty years; admitted February 16, 1906; discharged, well, March 18, 1906.

February 16. Entirely well until night. She had some muscular pain during night, and at 3 A.M. a hard shaking chill, followed by headache and severe muscular pains. No cough or expectoration. Physical examination entirely negative. Leukocytes, 11,500; temperature, 103° to 104°; pulse, 110 to 120; respirations, 26.

February 17. Leukocytes 12,700. Pain in head and neck.

February 19. Temperature has been gradually falling, and is now normal.

February 23. Yesterday, without discoverable cause, temperature rose again to 102°, and the patient again complained of headache and general soreness. Physical examination negative. Leukocytes, 15,300.

February 28. Another relapse, with fever 101°, general malaise, and soreness. A differential blood count is found normal. No malarial organisms.

March 7. After four days of normal temperature patient again has had a return of fever (102°) and all her previous symptoms. Leukocytes, 15,000.

March 18. Since last note temperature has remained normal and patient has made a rapid recovery.

CASE XI.—A. McV., twenty-three years; bricklayer; admitted April 8, 1906; discharged, well, April 27, 1906.

April 3. Moderate frontal headache, anorexia, constipation, general soreness, prostration, cough, with mucous expectoration.

April 5. Severe epistaxis. Pain in shoulders and knees.

April 6. Severe epistaxis. Chilly feelings, profuse sweats, pain in right chest.

April 8. Fever reached 104°.

April 9. Admitted to Hospital. Face flushed, tongue clean, looking sick, but physical examination showed nothing more. Temperature, 103.8°; pulse, 92; respirations, 24.

April 11. Feeling better. Some general soreness still. Cough, with free mucous expectoration. Temperature, 99° to 103.3.°

April 13. A small area of consolidation found in right middle lobe. Temperature, 101° to 103°.

April 15. After remission for forty-eight hours temperature rose suddenly to 102.5°. Pharynx congested. Inguinal glands swollen. No cause found for increase in fever.

April 16. Second sudden shoot of temperature to 103.5°. No cause found.

April 27. Temperature remained normal after last note, and patient made a rapid recovery.

The recognition of these cases is not, as a rule, difficult. They

belong to the winter season, when influenza is prevalent. They begin suddenly, usually with the characteristic symptoms, headache, general muscular soreness and pain, and prostration. They may have a cough and expectoration, and in the sputum the influenza bacillus may be found in large numbers.

It is now well understood that the presence of the influenza bacillus is not a frequent happening in the affection clinically known as influenza. The great majority of such cases do not show the influenza bacillus, but show pneumococci, streptococci, or staphylococci in large numbers in the sputum, if there is expectoration. Of course, also, many of the patients have no cough or expectoration. When, however, the organism can be found in the sputum in large numbers, the finding is of significance. The most characteristic feature of these cases is the exceeding irreguiarity of the temperature curve, as indicated in both these cases. The fever comes and goes in a most unaccountable manner. It is to be understood that in these cases the most careful watch must be kept to exclude the presence of complications which would explain the sudden rise and fall of the fever, such as acute otitis, mastoiditis, or involvement of the antrum or accessory sinuses. We must also recognize the fact that the fever may come and go independently of such complications. Regularly with the return or increase of the fever there is return or increase in the clinical symptoms. These patients regularly recover. In protracted cases outside of the hospital we often find that the best thing to be done for such patients is to get them out of the city.

The blood examinations in these cases have only moderate value; usually they show a slight or moderate leukocytosis ranging from 10,000 to 20,000. The differential counts, as in Case II, are all normal. Blood cultures are negative.

5. Unexplained Fever. The history of this patient is as follows:

Case XII.—M. S. G., aged thirty years; admitted May 10, 1907; discharged January, 1908.

History. Family: Negative. Personal: Born in Scotland; in Honolulu four years; in Trinidad one year. Menstrual: Amenorrhœa fifteen months. Previous: Measles, typhoid, dengue, tuberculosis three years ago, tonsillectomy, appendicectomy. Present: Cough, expectoration, constipation, nausea and vomiting, headache, syncope, increasing weakness. Abdominal pain and fever from January to admission.

Physical Examination. Negative except for a slight tenderness of left lower quadrant of abdomen.

From May 10 to June 1 the patient did well. She had one or two temporary rises of fever, but most of the time the temperature was within normal limits. All her symptoms cleared up, and except for constipation she felt well. From June to October she ran a continued fever of varying degree, for some days ranging from 100°

to 101°, but most of the time higher—101,° 102°, and 103°. There was an ebb and flow very suggestive of typhoid fever in the weekly curves, but none of the characteristic signs developed. There was almost constant leukocytosis, as the appended table will show, no Widal reaction, and negative blood cultures. The only suggestive thing about the physical examination was persistent tenderness over the left half of the abdomen, especially in the region of the left kidney. The urine was normal; an uncontaminated specimen was obtained and found sterile. The fever, leukocytosis, and persistent pain suggested a local suppuration, but the signs did not develop, and, the patient's condition remaining good, action was deferred. Finally, in the first week of October the fever gradually rose, and on the 10th reached 105°. With this rise there was a distinct increase in the local tenderness and pain, and an exploratory operation seemed demanded. This was done by Dr. McCosh, and a most thorough examination of the abdomen disclosed nothing abnormal whatever. Lest by any chance a minute focus in the kidney should be overlooked, the kidney was exposed through a lumbar incision and carefully examined. No lesion was found. The wounds were then sutured and the patient returned to the ward. The temperature at once fell, and within three days became normal and so continued. The patient rapidly regained her strength, and in a few weeks left the hospital quite well.

Blood Examinations.

	Hemoglobin. Per cent.	Red cells.	White cells.	Polynuclears. Per cent.	Transitionals. Per cent.	Large mononuclears. Per cent.	Small mononuclears Per cent.	Basophiles. Per cent.	Eosinophiles. Per cent.
May 10 . . .	70	5,600,000	15,100	76	3.5	10 5	8.3	0.8	1.0
June 9 . . .	...	.....	23,800						
June 10 . . .	...	.....	25,000						
June 24 . . .	...	.....	15,300						
July 27 . . .	...	.....	28,000						
July 31 . . .	...	.....	16,500						
August 2 . . .	...	.....	18,900	84	6.0	2.7	7.3		
August 12 . .	...	.....	13,000						
August 13 . .	...	.....	12,100						
August 22 . .	...	.....	10,000						
October 1 . .	70	4,500,000	25,000	90	1.0	6.0	8.0	0.25	0.25
October 4 . .	...	.....	17,000	76	1.0	2.0	20.0	.....	1.0
October 9 . .	...	.....	16,800						
October 10* . .									
October 29 . .	...	.....	15,000						

* Operation.

For this case we have at present no satisfactory explanation. The symptoms, the blood counts (the high percentage of polynuclears), and the course of the affection indicated the presence of some purulent focus. No such focus was found, yet the patient promptly recovered after operation. There was no suggestion of hysteria in the patient. Mentally she was entirely normal. Theoretically it may be possible that a minute focus of suppuration did exist in some part of the abdomen and that the circulatory changes induced by the operation brought about its cure, in some such way as laparotomy cures tubercular peritonitis; or possibly a minute focus was evacuated without detection.

Practically the case illustrates the fact that there are seen from time to time cases of protracted fever which cannot at present be satisfactorily classified.

SUMMARY. 1. Malarial fever is easily recognized by the presence of the characteristic microörganisms in the blood, and by its amenability to quinine. Fevers not conforming to these requirements are not malarial.

2. Typhoid fever can be recognized or excluded with equal accuracy by the combination of clinical and laboratory evidence.

3. Tuberculosis and sepsis of certain types present clinical pictures so closely similar that they can often only be differentiated by the ultimate outcome of the case, possibly only by autopsy.

4. Influenza may give rise to protracted fever, which can usually be easily recognized from the condition under which it occurs, sudden onset, characteristic symptoms, and course.

5. Sepsis in other cases may be clearly indicated by very high leukocyte counts, with high polynuclear percentages, before any localization of the process can be made.

6. Blood cultures are of very great value in the differentiation of fevers, especially in typhoid fever, and in such conditions as malignant endocarditis.

7. There are cases of long protracted fever which cannot at present be satisfactorily classified.

CERTAIN COMPLICATIONS OF PNEUMONIA.

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IN this paper I purpose dealing only with certain complications of pneumonia, some common, others rare, which have come under my notice, and of emphasizing certain lessons they have taught me. The first and most important lesson, which all the cases have forced upon me, is the well-known fact that pneumonia is a constitutional

disease, due, doubtless, to the effects of the pneumococcus upon the system: a true pneumococcemia. The second, which is a corollary of the first, is that to look upon the lung as the only organ affected is to be far from the mark of accuracy. Many, perhaps all, of the complications are but local manifestations of the general poisoning. Hence, if a patient is to be treated properly, each day from the beginning every organ must be watched, in order that any disturbance of its function may be recognized early and if possible corrected. Another lesson is, that some of the complications, or perhaps sequels, develop a longer or shorter time after the crisis or lysis. Some of these may be necessarily fatal, others, if recognized in time, are amenable to treatment. Hence the necessity of watchfulness after the acute symptoms are over.

Disturbance of the Renal Function. In my experience practically all cases of pneumonia which exhibit any serious constitutional disturbance show albumin and casts in the urine. The amount of albumin, the number of casts, and the amount of urine, are rather an index of the degree of poisoning than symptoms which are dangerous in themselves. One patient, however, a boy aged seven years, severely ill with involvement of one entire lung, had a veritable suppression of urine. The small amount passed was loaded with albumin and casts, and the patient suffered apparently from renal inadequacy. Other cases with less renal symptoms occur frequently. The urine, therefore, should be examined daily in every case, in order that we may anticipate any serious involvement of the kidney. The patient should be given an abundance of water. A prescription composed of: Spirit of nitrous ether, 3 drams; potassium citrate, 2 drams; lemon juice, 4 drams; and water sufficient to make 3 ounces, of which two teaspoonfuls should be given every two hours, often has the effect of causing a more abundant flow of urine and consequent comfort to the patient. If there is true suppression, dry cups to the loins, and the administration of nitroglycerin in full doses will be of the greatest value. A case on record in which a true nephritis with total suppression of urine occurred, responded promptly to infusion of digitalis.

Disturbance of the Digestive Organs. In severe cases of pneumonia, there is always more or less abdominal distention, due to intestinal paresis and to the formation of gases in the intestine. In some cases this abdominal distention is a veritable complication, being so great that the respiration and the heart action are seriously interfered with. One fatal case of the most severe poisoning that has been my fate to see, occurred in a lad aged nine years. Diarrhœa and abdominal distention were as great as in any case of typhoid fever I have observed. Nothing relieved it. Usually attention to food, milk being, as a rule, best borne, will correct the conditions. When milk itself disagrees, albumen water alone, or nothing but plain water should be given. Physostigma or eserine should be

tried, but in my hands is of little value. Salol and sodium bicarbonate, either in a combination or singly, have been the best drugs. Vomiting is troublesome in some early cases, but simple limitation of food will usually control this. There is but little danger of the patient suffering from the lack of food.

Middle ear disease is common, sometimes giving rise to mere deafness, sometimes to suppuration and its consequent dangers. The ears should be constantly examined, especially when the patient is unconscious, in order that an otologist may be summoned and the drum punctured when it shows redness and bulging. When suppuration occurs, the meatus should be kept clean by wiping with cotton and, toward the end, insufflation of boric acid.

In some cases this complication is due to the pneumococcus, in others it is the result of a simple nasopharyngeal catarrh, which is either a forerunner, or an accompaniment of the attack of pneumonia. Neglected suppuration of the middle ear, if it be due to the pneumococcus, leads occasionally to that most fatal complication, meningitis.

Cardiac Dilatation. In a certain number of cases, notably in drunkards, or in individuals whose heart musculature is weak, cardiac dilatation occurs, and is almost always fatal; it may occur when the patient is apparently doing well. The following is a typical example:

Wm. L., aged seventy-five years, was seized with a chill on December 29, 1899. On January 1, 1900, there was complete consolidadation of the lower left lung. His temperature was 102°, and his pulse 96. The heart dulness was normal. The first sound of the heart was weak. On January 2, 1900, the consolidation of the lower lobe was complete. A sphygmographic tracing showed a pulse of extremely low tension, resembling that of aortic regurgitation. Suddenly, on the morning of January 3, there was rapid respiration, feeble, rapid pulse, and the entire chest became full of rales, and the area of cardiac dulness greatly increased.

Such cases are common enough. Two things are of paramount importance: (1) Absolute rest, in a recumbent posture, the patient using the urinal and the bedpan. If this rest is made imperative, there will be fewer cases of absolute sudden collapse. (2) The necessity of listening to the heart and percussing its area daily. This can be done with very little annoyance to the patient. It is of value, because usually, but not constantly, the heart dilates gradually, and this dilatation is seen in the weakened first heart sound and in increase of the area of cardiac dulness. When these signs are noted, and especially when accompanied by an increasing pulse rate, the time has come for the free use of digitalis and whiskey. When the sudden collapse is upon us digitalone and morphine hypodermically are our sheet anchors. The morphine quiets the patient and apparently stimulates the heart. Albuminuria is not

a contra-indication to its use. The use of the blood-pressure instrument is of value. If the pressure is high, nitroglycerin is of value; if low, stimulants, digitalis or digitalone, should be given. Inhalations of oxygen seem to relieve the dyspnœa, but are rarely necessary when the patient is treated in the open air.

Pericarditis and endocarditis may both occur in a small percentage of cases. Those which have come under my care were the expression of most severe systemic poisoning, and the majority have been fatal. The first case was that of a young woman, aged twenty-three years, who suddenly developed consolidation of the entire right lung and later pericarditis and endocarditis. This case ran a furious course and ended in death in a few days. Another case has recently been under my care at St. Timothy's Hospital. The patient, a woman, aged forty years, was admitted on the evening of March 23, 1908, with what was supposed to be rheumatism. Her temperature was 99.2°. By morning she was complaining of severe precordial pain and was restless. Her temperature at my visit at noon was 100.6°. On examination, the heart dulness above and to the right was normal. There was a very marked to-and-fro friction rub. There was consolidation of the entire lower lobe of the left lung. The patient became rapidly weaker. The temperature never rose above 103°. The heart gradually dilated and the patient became markedly cyanosed, and died on the fourth day after admission. In this case ice-bags to the precordium gave more relief than any other measure. Manifestly the treatment of this condition, when due to a local manifestation of the pneumococcic involvement, must be entirely symptomatic. Morphine was used with apparently good effect, but did not give as much relief as the ice.

Arthritis. This same patient developed the very rare condition, arthritis. Practically every joint of all the extremities was involved. On the day after admission she complained bitterly of pain in her knees. Both knees were swollen and red. The next day the swelling was less in the knees, but the arms were affected. On the day before death every phalangeal joint of both hands was swollen, dark, dusky red, and exquisitely painful. The fingers and hands were in a semiflexed position and could not be used by the patient. No culture was made from the joints, but the condition seemed the direct result of the systemic poisoning. Treatment was of no avail, although the pain was relieved by wrapping the hands in cotton.

A rare complication, which I do not see noticed in Musser and Norris' recent article,[1] is gangrene of the extremities. A case of this condition was seen by me with Dr. Simcox, to whom I owe the privilege of this report. The patient was a male, aged forty-one years. He was an alcoholic. He was seen November 5, 1906, with a temperature of 103°, pulse 120, and respirations 48,

[1] Osler's Modern Medicine, 1907, vol. iii.

with complete consolidation of the right lung. Contrary to expectation, resolution of the lung occurred, and on November 8 the temperature was normal. It remained normal until November 10, when it suddenly rose to 103.2°. On November 11 the following note was made: There is very marked œdema of both hands and cyanosis of the tips of the fingers of both hands. There is no cyanosis of the lips. There is also cyanosis of the lower half of both forearms, with true petechiæ along the lines of the superficial veins. In the afternoon of the same day the fingers were black and almost gangrenous. The toes were normal.

On November 12, 1906, this note was made: The tips of the fingers are black, cold, and shrivelled to the first joint. The rest of the hand is swollen, warm, and mottled. The gangrene advanced, and the patient died on November 13. The temperature was high until death.

The following is the postmortem note: From the middle of the forearm downward there is a bluish-black discoloration. The tips of the fingers are black, shrivelled, and dry. The radial artery, the ulna, both palmar arches, and two interossii with their digital branches were removed. The arteries are not atheromatous. There is a firm thrombosis filling the interossii to a distance one inch proximal to the digital division, and completely filling the digital branches. Apparently the thrombosis began in the terminal arteries and had advanced upward.

Meningitis may be the result of general poisoning, or it may be the direct result of a local ear condition. As an instance of the former may be cited the case of a lad, aged four years, who was admitted to St. Timothy's Hospital suffering from supposed typhoid fever. There were marked symptoms of meningitis, stiff neck, Kernig's sign, and a *tache*. A lumbar puncture was made and a slightly turbid fluid withdrawn. A diplococcus lying outside of the rather numerous polymorphonuclear cells was demonstrated. Examination later showed areas of consolidation throughout the lungs. The child died, and at the autopsy a meningitis and a consolidated lung were found. Pneumococci were found in the meninges and in the lung. In this case the meningitis was doubtless the initial effect of the pneumococcus.

A second case was also seen in St. Timothy's Hospital: The patient, aged fifty-three years, was admitted February 16, 1908, in the first twenty-four hours of what proved to be a most serious attack. The lung involvement began at the right base, but rapidly involved the whole right lung. The fever never went above 103°, and reached that point but once. The entire temperature range was low. Resolution occurred, delirium disappeared, and the patient seemed about to recover. Gradually, however, she became dull mentally, and on March 3 it was difficult to arouse her. On March 5 the neck was stiff. There was a seropurulent discharge from

the left ear. On March 6 there was distinct retraction of the head, together with dilatation of the left pupil. Eye-ground examination was negative. A spinal puncture was done with the hope of giving relief, but the patient died on March 6, with a sudden rise of temperature to 104°. The temperature had remained practically normal until the morning of March 5.

Pleuritis. By far the most common serious complications of pneumonia in my personal experience are pleurisy with effusion and empyema. Both of these conditions can surely be diagnosticated, if care is taken in comparing the symptoms with the physical signs. Nothing is more distressing than the discovery of an empyema days or weeks after an attack of pneumonia. The condition is constantly diagnosticated unresolved pneumonia, typhoid fever, malaria, etc. The mistake in diagnosis is usually due to the fact that the physician in charge has failed to strip his patient and simply look at the chest. In walking the ward of Johns Hopkins Hospital in company with other physicians, and under the charge of Osler, the following occurred: Osler came to a bed containing a child who had just been admitted, and whom he had never seen before. He threw back the bedcovers and revealed a girl about seven years old, emaciated in the extreme, the left chest bulging, and the cardiac impulse in the region of the right nipple. Osler remarked: "Gentlemen, if you treat your cases like this, at the last day St. Peter will confront you with a line of little children who will point their fingers at you and exclaim, 'You sent us here before our time because you did not take the trouble to examine our chests.'"

Every case of pneumonia should receive a careful physical examination after the crisis, to be repeated until a diagnosis is made, if the patient is not doing well. There is no possible excuse for failure to make those repeated examinations, although a diagnosis may be difficult. The following cases well illustrate my point:

L. J., aged eleven years, was sent to me from Tamaqua, with a diagnosis of appendicitis. His temperature was 102°. His attack had begun two days before with sharp pain referred to McBurney's point. On examination, March 3, the belly was flat, there was slightly more resistance on the right side. There was no tenderness. There was decided dulness over the lower lobe of the right lung. There was blowing breathing at this situation. On March 9 the breath sounds became much less marked and the cardiac dulness was well beyond the nipple line. Signs of effusion over the consolidated area gradually increased. On the 13th the temperature was normal, and remained about 99° until recovery. On the 14th the whole right chest was flat; there was no blowing breathing. The patient was tapped and about six ounces of serum was removed. The patient left the house well on March 25.

A second case, which shows the difficulty of locating the purulent material, is the following:

L. C., aged sixteen years, was admitted October 27, 1900. His temperature remained 103° for five days. It then dropped to normal and remained there for three days. On November 11 he began to have a slightly irregular fever. The fever gradually increased. On December 2 the breath sounds were much less marked over the consolidated area. A needle was inserted and run in all directions, but failed to show the presence of pus. So certain were we by this time that there was a collection of pus in the chest that the patient was urged to undergo surgical exploration of the chest. This he refused. On December 18, after going to his home, he had a severe coughing spell and expectorated a very large quantity of pus. Fortunately, the cavity did not refill, and the patient entirely recovered.

A third case of interest in still in the surgical wards: Geo. Mc., aged eighteen years, was admitted March 14, with consolidation of the lower lobe of the right lung. This very rapidly increased until the whole lung was involved. He was very seriously ill, but on March 22, the temperature reached normal by lysis. It remained normal until April 9, when it began to oscillate. Careful examination showed the whole right chest filled with subcrepitant rales. On the left side, the lung which was not affected by the pneumonia, there was dulness over the entire base on a line horizontal to the nipple. There was no tactile fremitus and no breath sounds nor voice sounds. A needle inserted showed a collection of pus. Resection of the rib was done, and the patient is now about well.

The lesson to be learned from these cases is: Make a careful physical examination during and after the attack. If the temperature does not soon reach normal and remain there, daily examination should be made to search for areas of dulness. When an area is found which is thought to indicate the presence of pus, a large, long needle should be inserted. If pus is found, of course, rib resection must be made. In cases in which the physical signs and symptoms warrant the diagnosis of a collection of pus, and the needle does not show its presence, I feel that an exploration of the chest by a surgeon is not only justifiable but mandatory. It is waste of time and dangerous to play with drugs under these circumstances.

All the cases cited show the necessity of eternal vigilance on the part of the physician, and the necessity of employing modern methods of diagnosis and treatment.

INFLUENZAL MENINGITIS.

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Since the discovery, in 1892, by Pfeiffer, of Bacillus influenzæ, there has existed in the minds of many bacteriologists some doubt as to the specificity of the organism. Contrary to the original observations of the discoverer, the bacillus could be found in inter-epidemic periods without an associated influenza. Moreover, it did not seem possible to reproduce the disease experimentally in animals. The fact that in the meningeal type of influenza, usually a fatal disease, a pure culture of the bacillus can be obtained from the spinal fluid, which, when injected into the meninges of animals, will produce an acute meningitis, affords, perhaps, the best confirmatory evidence we have of the pathogenicity of the organism. Meningitis, due to the influenza bacillus, while at present regarded as a rare manifestation of influenza, will doubtless, with more careful bacteriological study of the cerebrospinal fluid, in the future prove to be a much more common affection than present statistics indicate. The case here reported is of interest on account of its occurrence in an adult and of the termination in recovery.

D. R., a male, aged thirty-three years, was admitted to the service of Professor Barker in the Johns Hopkins Hospital, June 15, 1907, showing signs of meningeal irritation. The personal history of the patient was unimportant except for an injury, two weeks previously, caused by a blow from a bottle above the left ear, following which the patient had remained in bed complaining only of dizziness and cold in the head.

On admission the patient was found to be extremely restless and at times delirious. The neck was held stiffly, with some retraction, and when flexion was attempted the patient raised the whole body in defense. There was a very marked Kernig sign present on both sides. Both eyes were kept closed and the right eye showed a slight external strabismus. The pupils were small and equal, and reacted actively to light. There was no evidence of an acute rhinitis. A crop of herpes was noted at the right commissure of the mouth. An incised wound was found above left ear, evidently only a scalp wound. The heart and lungs were found normal. The spleen was not enlarged. The knee-jerks were active, and plantar stimulation yielded plantar flexion of the great toes. The aural examination gave evidence of chronic middle-ear catarrh of both ears. The ophthalmoscopic examination showed both disks to be very hyperemic, œdematous, and slightly swollen. The arteries and veins were large and the veins quite tortuous. In the upper part of the right disk the remains of a small hemorrhage was seen.

Lumbar puncture was performed on the day of admission. The fluid obtained was very slightly turbid and yielded a pressure of 400 mm. Hg. After the removal of about 30 c.c. the pressure equalled 150 mm. Hg. Two subsequent punctures were made, from both of which a turbid fluid was obtained under increased pressure.

The temperature on admission was 101.5°. For about eight days a fastigium of 100° to 104° was maintained. The pulse at this time, in contrast, was slow, from 64 to 95 to the minute. The temperature and pulse chart simulated closely that of typhoid fever. During the second week the morning remissions of temperature became more pronounced, with an evening elevation of 3° or 4°. On the fifteenth day after admission the temperature fell to normal and remained so except for a sharp rise to 104.5° after three days of normal temperature. The temperature following this elevation quickly fell to normal and remained so. The pulse rate was slow throughout the entire course of the disease, at times being only 50 to the minute. The blood pressure remained slightly below normal during the course of the disease, averaging 108 mm. Hg. The respirations on admission were 24 to the minute, never rising above this. They fell gradually after four days and remained at 18 to 20 to the minute.

The erythrocytes showed a fairly high count, 5,304,000 per c.mm. The hemoglobin measured 105 per cent. (Sahli). The leukocytes on admission were on the upper limit of normal, 9800 per c.mm. Four days later they had risen to 13,000. Another count made still four days later showed 13,120 with the following differential findings: Polymorphonuclears, 87.5 per cent.; small mononuclears, 9 per cent.; large mononuclears, 3 per cent.; and eosinophiles, 0.5 per cent. Toward the end of the disease, as the temperature reached normal, there was a fall in the leukocyte count. On July 18, the day on which the temperature fell to normal, the leukocytes were 10,760. After six days of normal temperature the leukocyte count was normal at 8060.

During the first four days there was retention of urine and catheterization was necessary. On admission the urine was high colored, had a specific gravity of 1027, was acid in reaction, and contained a heavy cloud of albumin. Microscopically a few hyaline and granular casts and cylindroids were found. Two weeks later a faint trace of albumin still persisted, but the casts had disappeared. Before the patient left the hospital both albumin and casts were absent. Convalescence was rapid and complete, and the patient was discharged well on the thirty-fourth day.

Bacteriological Report. The cerebrospinal fluid obtained from the first lumbar puncture was very slightly turbid, containing a few flocculi. Smears made from the centrifugalized fluid and stained with methylene blue showed many polymorphonuclear cells and a very few diplobacilli, sometimes only two in a field; some of these

were extracellular, while a few were seen enclosed within the polymorphonuclear cells. The organisms were best stained by a dilute (1 to 10) aqueous solution of carbol-fuchsin. Cultures were made on blood agar, plain agar, glycerin agar, blood serum, and other laboratory media. After forty-eight hours on blood agar, along the streak of the needle, could be seen a delicate growth of small pinpoint colonies of dew-drop appearance. The colonies were non-hemolyzing and showed a tendency to remain discrete. The other media remained sterile. Transfers to pigeon-blood agar gave a luxuriant growth of dew-drop colonies, while sub-cultures on hemoglobin-free media yielded no growth. Morphologically the growth showed a short, thick bacillus, resembling a diplobacillus, which was non-motile and Gram-negative, and stained best with dilute carbol-fuchsin and well with Bismarck brown. The culture, which was a pure one, conformed in every respect biologically and morphologically with the bacillus of Pfeiffer.

The same bacillus was also obtained in the fluid from the second lumbar puncture. In the smears from the third puncture it was noted that there were more intracellular organisms, and fewer extracellular than formerly. A pure culture of influenza bacillus was again grown from the fluid of the third puncture.

Two blood cultures were made: one on the day of admission, and a second eight days later. Ten cubic centimeters of blood, taken from the median vein was divided among six agar plates. Both cultures yielded negative results.

The agglutinating power of the patient's serum for the organism obtained from the spinal fluid was tested. A suspension of the bacilli grown upon pigeon-blood agar was used with 1 to 10 dilution of serum. There was some clumping at the end of an hour; there was clumping also with higher dilutions, but the extent of this clumping was not appreciably greater than that found in the controls used. It could not be shown that the serum possessed specific agglutinins. Animal inoculation was also without result. The infection could not be reproduced with repeated injections of an emulsion of the bacilli into the ear veins of a rabbit.

Historical. The number of cases of influenzal meningitis reported in the literature, in which a precise diagnosis has been made from exact bacteriological findings, is extremely small in comparison with the epidemic character of influenzal infection. I have been able to collect twenty-four cases in which the bacteriological reports may fairly be regarded as trustworthy. Many cases have been reported in which the proof of the identity of the organisms has not been convincing. As early as 1892, following the pandemic of 1899 to 1890 and the discovery of the influenzal organism by Pfeiffer, Pfuhl[1] described three cases of meningitis in

[1] Deut. med Woch., 1895, Nr. 25; Berl. klin. Woch., 1892, xxix, 979; Deut. med. Woch., 1896, xxii.

which he regarded the influenza bacillus as the etiological factor. Later the same author added eleven additional cases to the literature. All of his cases, however, showed a mixed infection or uncertain bacteriological findings, and cannot be accepted as positive cases of influenzal meningitis.

Haedke,[2] in 1897, reported a case of purulent meningitis from which, at autopsy, the influenza bacillus was grown along with some putrefactive bacilli, regarded by the author as due to postmortem infection. Fraenkel[3] a year later added two cases, both of which occurred in infants. At autopsy in each case a pure culture of the influenza bacillus was obtained from the meningeal exudate. To Slawyk[4] is due the credit of having first established an exact diagnosis intra vitam of an influenzal meningitis by means of lumbar puncture. Prior to him Testivin[5] had performed lumbar puncture upon a patient with Pott's disease, who developed meningeal symptoms, and reported the finding of influenza bacilli, regarding the case as one of influenzal meningitis. The report, however, must be accepted with doubt. A case reported by Langer[6] is of interest as being the first recorded in which recovery has followed an attack of influenzal meningitis. Following these earlier observes, Meunier,[7] Ghon,[8] Trailescu,[9] Dubois,[10] Thomesco and Gracoski,[11] M. Simon,[12] and Caccia,[13] have each contributed cases to the literature. In 1903 Mya[14] reported no less than four well-authenticated cases of influenzal meningitis, all of which occurred in infants. The author in his report expressed the opinion that the influenza bacillus is equally important with the meningococcus or the pneumococcus as the casual agent of meningitis in infants. In the year following Bertini[15] and Jundell[16] reported one and two cases respectively. Dudgeon and Admas[17] have observed a case of pyemia, which they regarded as due to the influenza bacillus and in which there was an associated multiple arthritis and meningitis. The primary focus was believed to be an epiphysitis of the upper end of the radius. The author stated that a pure culture of Bacillus influenzæ was obtained in the pus from the elbow, from the spinal fluid, from an abscess about the hip-joint, and from the splenic juice. Douglas[18] in the same year (1907) reported a case which he cites as the first case observed in England in which the organism was obtained in pure culture from the cerebrospinal fluid during life, and from the meningeal exudate at autopsy. Adams,[19] also during the same year,

[2] Münch. med. Woch., 1897, xliv, 806.
[3] Ztschr. f. Hyg., 1898, xxvii,315.
[4] Ibid., 1899, xxxii.
[5] Dauphiné medical., 1897, xxii, 49.
[6] Jahrb. f. Kinderheilk., 1901, liii, 91.
[7] Compt.-rend. d. soc. de biologie, 1900, 5.
[8] Wien. klin. Woch., 1902, xv, 667.
[9] Ref. in Münch. med. Woch., 1902, 118.
[10] Thèse de Paris, 1902.
[11] Abs. in Révue neurologique, 1905, 44.
[12] Cited by Dubois, Thèse de Paris, 1902.
[13] La Pediatria, 1903, 172.
[14] Gaz. degli osped., 1903, xxiv, 269. Riv. di clin. pediatrica, Firenze, 1903, i, 465.
[15] Riv. di clin. pediatrica, Firenze, 1904, ii, 673.
[16] Jahrb. f. Kinderheilk., 1904, lix, 777.
[17] Lancet, 1907, clxxiii, 4384.
[18] Ibid, January, 1907, 86.
[19] Archives of Pedriatrics, New York, 1907, xxiv, 721.

reported a case which he stated to be the first recorded in America, in which the clinical diagnosis of influenzal meningitis was confirmed by the finding of the Pfeiffer bacillus in the spinal fluid. A second case reported by Spriggs,[20] was believed to be due to the influenza bacillus. In France during the same year Carles[21] reported an additional case.

A number of observes have published reports of cases of influenzal meningitis in which the Bacillus influenzæ, carefully identified, has been found associated with some other microörganism in the spinal fluid intra vitam, or in the meningeal exudate at autopsy. With such mixed infection it is impossible to state which is the dominant organism, and the cases cannot be regarded as of purely influenzal etiology. Such reports have been made by Peucker,[22] Högerstedt,[23] Nuttall and Hunter,[24] Hecht,[25] Ghon,[26] and G. L. Simon.[27]

In a third group must be placed a number of cases reported in the literature as influenzal meningitis, in which the bacteriological studies have been incomplete, or of such a nature as to leave doubt concerning the identity of the organism. The reports of Cormil and Durante,[28] Gioelli and Zirolia,[29] Bury,[30] Rendu[31] and Carlini[32] are of this nature. In still another class may be mentioned the reports of influenzal meningitis in which the diagnosis has been made wholly upon clinical evidence. Since a precise diagnosis is possible only by the bacteriological examination of the spinal fluid, such reports are obviously worthless in a statistical study of the disease.

Pathological Anatomy. The greater number of the cases of influenzal meningitis reported in the literature have come to autopsy. The pathological lesions found have been of a nature similar to those of meningitis due to the meningococcus and pneumococcus. So faithful has been the resemblance that such good observers as Fraenkel and Ghon have believed it impossible to distinguish, either macroscopically or microscopically, meningitis of influenzal origin from the meningococcal or pneumococcal forms.

One interesting condition found in this form of meningitis is the extreme variability in the localization of the lesions, dependent in some measure upon the portal of entry of the invading organism. The dura mater may be found infiltrated throughout its entire extent, forming a diffuse meningitis, as in the case of Meunier. In other cases the involvement is not uniform, and distinct zones may be found free from the purulent exudate. In such areas the dura is firm and brilliant. Where the dura has been covered with pus, it

[20] Amer. Jour. Obstet., 1907, lvi, 467.
[21] Jour. de med. de Bordeaux, 1907, 106.
[22] Prager. med. Woch., 1901, xxvi, 153.
[23] St. Petersburg med. Woch., 1895.
[24] Lancet, London, June 1901, p. 1524.
[25] Jahrb. f. Kinderheilk., 1903, lvii, 333.
[26] Wien. klin. Woch., xv, 1902, 667.
[27] Rev. mens. de mal de l'enf., 1905, xxiii, 271.
[28] Bull. de l'academie de médecine, 1895, 469.
[29] Cited in Centralblatt, f. path. Anat., 1901.
[30] Brit. Med. Jour., 1900, ii, 877.
[31] Bull. et men. de la soc. med, des hôp. de Paris, 1901.
[32] Riv. di clin. pediatrica, 1907, v. 42.

is thickened and opaque. Microscopically an enormous infiltration of the tissue is found. The appearance of the pia mater is similar, being found almost normal in certain areas, where a deposit of pus has not taken place. In the regions where the pus is abundant the pia has a dull aspect and the vessels are much congested.

The surface of the brain is usually flattened, especially over the areas where the purulent exudate is most abundant. The lesion may be greater at the base of the brain where the cerebrospinal fluid is most abundant, as in the cases of Fraenkel, Haedke, Slawyk, and Ghon. In a second case reported by Fraenkel the lesion was most prominent over the posterior extremity of the right hemisphere. The inferior surface of the frontal lobe was found attacked, in an observation made by Haedke. The lesion, again, may be almost unilateral. In one of Ghon's cases a fibrinopurulent leptomeningitis of the right cerebral hemisphere was found. The convolutions in the affected areas may be so thickly covered with the exudate as to efface the sulci and fissures. The deposition of pus is usually greatest along the course of the vessels. The ventricles, as a rule, are dilated and filled with a serous or seropurulent fluid, sometimes reaching a purulent condition, as in the observations by Fraenkel and Slawyk. An acute hydrocephalus is not uncommon. The tela choroidea was found infiltrated with pus in the cases reported by Bertini and Douglas. The cortex and medulla may be found without change. Small focal hemorrhages are not uncommon. The gray matter was found softened in the case of Douglas.

The pathological picture is more uniform in regard to the findings in the cord. A diffuse meningitis, with lesions predominating over the dorsal surface of the cord, is the rule. The cord itself usually escapes, although in some cases a myelitis has been found. The anterior surface of the cord may be found free from inflammatory exudate (Douglas).

The exudate presents varying aspects. In general it is thin, of a greenish-yellow color, and of gelatinous consistence; at times it may be simply serous. The deposition is more or less uniform and is increased along the course of the vessels. It is found most abundant upon the inferior surface of the brain, and over the dorsum of the cord, a condition not improbably due to the decubitus of the patient. The pus, as a rule, is inodorous, although a fetid condition has been described.

The cerebrospinal fluid is usually turbid. At times, however, it may be so clear and transparent as to suggest a meningitis of tuberculous origin. In other cases it is purulent. The sediment is invariably rich in polymorphonuclear cells. In our case 1306 cells per c.mm. were found, of which about 76 per cent. were polymorphonuclears. The fluid is always under increased tension. A pressure of 400 mm. was noted in our case at the first lumbar puncture; 280 mm. at the second, and 250 mm. at the third puncture. In

Slawyk's case the pressure measured 450 mm. The protein content is also increased, being 1 per cent. in Bertini's case. In Bury's case the sodium chloride content was estimated at 0.78 per cent. and the freezing point of the fluid was found to be —0.75°. Slawyk determined the toxicity of the fluid, and found 0.5 c.mm. to be lethal for a guinea-pig in thirty minutes.

The occurrence of the bacilli in the pathological lesions has been variously described. Fraenkel maintained that the causal agent is found only in the exudate, and is without any relation to the meninges and cerebral tissue. Pfuhl states that the bacilli are found disseminated throughout the neuroglia, in the lymph channels, in the interstitial cellular tissue, and in the blood capillaries. In Slawyk's case the bacilli were found generally distributed throughout the whole body: in the fluid of the left ventricle, in the blood, in the lungs, even in the smallest bronchi and alveoli, but not in the nasal secretion. The heart is usually found normal. There may be cloudy swelling of the heart muscle; at other times a dilated heart. Cloudy swelling of the liver and kidneys is commonly found. The lungs may be normal, or present the lesion of an acute bronchitis, or bronchopneumonia. Pleuritis has been found. Empyema of the frontal sinuses and the maxillary antrum and, more frequently, otitis media have been described.

Bacteriology. Since the influenzal nature of a meningitis can be demonstrated only by the identification of the influenza bacillus in the cerebrospinal fluid, a careful bacteriological study of a suspected case is of primary importance. The bacilli can be found in the fluid intra vitam, by means of lumbar puncture, or in the meningeal exudate at autopsy. The recognition of the organism is by no means easy. The spinal fluid may appear quite normal, and unless careful search be made the bacilli may be overlooked in smears. It is for this reason important that routine cultures from the spinal fluid be made on hemoglobin-containing media in all suspected cases, since otherwise, with ordinary media, the cultures may be reported as sterile.

The bacilli were first found in the cerebrospinal fluid during life by Slawyk; following him a number of other observers have obtained pure cultures of the bacillus in cases of influenzal meningitis. Cultures of the bacillus, mixed with other microörganisms, have been obtained by several observers. At autopsy the bacilli have been grown from the pus of the meningeal exudate, from the ventricular fluid, and from other parts of the body in cases in which a general infection was associated with the meningitis. Dudgeon has reported the growth of a pure culture of influenza bacilli from the pus of an epiphysitis involving the elbow, from an abscess about the hip, and from the splenic juice.

Pfeiffer found that the bacilli grew best upon pigeon-blood agar, a fact which he regarded as due to the instability of the pigeon

corpuscles, which allowed the hemoglobin to diffuse more readily into the media. Cantani[33] demonstrated that the bacilli will grow symbiotically upon spermatic fluid, and many other hemoglobin-free media, and hence regarded the globulin as the constituent favoring growth. Ghon, however, has shown that the media which Cantani used is not entirely free of hemoglobin. Davis[34] was able to grow influenza bacilli on media containing an infinitesimally small amount of hemoglobin, as little as 1 part in 180,000. The bacilli apparently multiply favorably in the cerebrospinal fluid.

In the smears made from the centrifugalized fluid in a case of influenzal meningitis, the bacilli may be numerous, or only a few may be seen in each field, occurring as short small rods with rounded ends. The length is about two or three times that of the breadth, usually 0.2 to 0.3 μ by 0.5 μ. They stain best with dilute (1 to 10) watery carbol-fuchsin. They may be found intracellular or extracellular, and are Gram-negative. At times prolonged search of a smear may be necessary to reveal their presence.

The culture on blood agar after twenty-four to forty-eight hours shows a delicate growth along the streak of inoculation of small, non-hemolyzing, dew-drop colonies, pin-point in size. The colonies tend to remain discrete, are oval or circular in outline, and have no central nucleus. They grow best at 36° to 38° C. Transfers may be grown on hemoglobin-containing media, but sub-cultures on ordinary media remain sterile.

PATHOGENESIS. There has been considerable experimental work done by various observers which seems to show that the cerebrospinal fluid affords an excellent nutrient medium for the growth of the influenza bacillus, and that the central nervous system is to be regarded as a locus minoris resistentiæ for the organism. Animal experimentation, on the whole, has not met with marked success in so far as the production of a general infection with the organism is concerned. Pfeiffer, himself, in a series of many experiments on mice, rats, guinea-pigs, rabbits, hogs, cats, dogs, and monkeys was unable to cause a true infection. In apes alone could an infections process be induced. In the other animals death could be produced only through the toxin. Jacobson found that an increase in virulence resulted when the influenza bacilli were injected into animals along with a culture of streptococcus. Many other observers have attempted to produce a general infection in animals, but the results have been almost invariably unsuccessful.

Cantani attacked the problem of infection in a new way, believing that in order to insure results the infectious agent should be transferred directly to the site of the organ to be studied. He experimented at great length upon the action of the bacilli in the central nervous system. After demonstrating that the role of trauma, due to the introduction of a foreign substance into the cavum cranii is

[33] Ztschr. f. Hyg., 1896, xxiii.

[34] Jour. Infec. Dis., 1907, xxiv, 73.

an insignificant one, be injected cultures of the influenza bacillus into the brain substance directly. With a large dosage in rabbits, the temperature, after eight to ten hours, rose to about 42° C., falling again after twelve to eighteen hours to normal or sub-normal. Dyspnœa with clonic spasms, followed by paralyses beginning in the hind limbs and quickly spreading over the whole body, terminating in death, formed the clinical picture. When the dose was not lethal signs of chronic meningitis soon developed. At autopsy the meninges were found strongly hyperemic, thickened, and cloudy, with a bloody serous exudate. The brain was also hyperemic, and the ventricles contained often a purulent exudate, in which the influenza bacilli were found microscopically and culturally. In microscopic sections the bacilli were found in the brain substance, and appeared to spread through the lymph vessels, being found in the lymph capillaries. In the cord the bacilli could be traced as far as the cauda equina, and they appeared to spread from the central canal into the gray matter. He concluded that the brain of the rabbit is a good nutrient substratum for the growth of the influenza bacillus.

His work with the toxins of the influenza bacillus was none the less interesting. Prior to him Pfeiffer had shown the toxin to be an intracellular one, bound up in the cell life. Cantani demonstrated that this endotoxin is in the highest degree toxic for the central nervous system, and that from 2 to 6 mg. of the dead bacteria is sufficient to kill an animal of 1500 to 2000 grams. He found experimentally that the action of the toxin of the influenza bacillus upon the central nervous system, as compared with toxins of other bacteria, is extraordinarily great. The inoculation of 12 mg. of a killed culture of cholera vibrio, 6 mg. of Bacillus coli communis, 6 mg. of Bacillus pyocyaneus, 9 mg. of Bacillus typhosus, or 9 mg. of Staphylococcus aureus in various animals caused no marked symptoms, while a dosage of 6 mg. of influenza bacillus was lethal.

Slatineano[35] was able to extract from cultures of influenza bacilli what he believed to be an endotoxin which was lethal for guinea-pigs upon injection into the brain substance, but had little action when injected into the peritoneum, showing the greater susceptibility of the central nervous system.

It has not as yet been certainly demonstrated that the serum of an infected patient contains agglutinins for the influenza bacilli. Cantani claims to have found that the agglutinating power of the serum of an immunized animal may be present up to a dilution of 1 to 500. Lord[36] in a series of such experiments found that the necessary dilution was low, that the reaction was very inconstant, and that the serum of apparently uninfected individuals also produced clumping. A positive agglutination reaction could not be obtained with the serum of our patient.

[35] Compt.-rend. d. soc. de biologie, lix, 339. [36] Osler's Modern Medicine, vol. ii, p. 469.

The question of the portal of entry of the influenza bacilli into the central nervous system has been the subject of much interesting discussion. By far the most common type of influenza is the respiratory one, characterized by acute rhinitis and bronchitis. This fact suggests the nasopharynx as a probable portal of entry. Fraenkel is an advocate of the hypothesis that the bacilli are conveyed from the lymphatics of the nasal fossæ, which in turn communicate with those of the meninges through the cribriform plate of the ethmoid, spreading thence directly into the cavum cranii. The theory is plausible, but at autopsies in almost all the cases of influenzal meningitis, the nasal fossæ have been found for the most part normal, and only rarely could a culture of influenza bacilli be grown from the nasal secretion.

The middle ear is also a likely portal of entry, especially when one considers the frequency with which otitis media develops as a complication or sequel of influenza, and how commonly influenza bacilli have been found in the pus of otitis media. At the Otological Congress in Bonn, in 1894, Hartman and Konel stated that they had found influenza bacilli in 90 per cent. of the cases of otitis media of influenzal origin in infants. Cheatle[37] believes that meningitis may be produced by infection from the middle ear, being carried along the vessels which pass through the remains of the petrosquamosal suture from the antrum to the middle fossa, without direct extension of caries. Posteriorly a middle-ear abscess may perforate through the bony portion which separates the mastoid cells from the lateral sinus, giving rise to an extra dural abscess in the posterior fossa, and it may thence extend farther, causing meningitis, thrombosis of the lateral sinus, or cerebellar abscess.

A general infection with the influenza bacillus must also be considered as a possibility in the production of meningitis. Several observers have been able to grow the bacillus from the circulating blood, and a multiple localization of the infection is conceivable. Slawyk regarded his case as one of general infection.

The primary foci of infection in the cases reported in the literature have been diverse. Ghon found a frontal sinus infection as the probable primary focus. The case reported by Headke was secondary to an otitis media, and influenza bacilli were found in the middle-ear pus. In Hecht's case the onset was preceded by an influenzal pneumonia of the right upper and lower lobe. Fraenkel believed acute rhinitis and bronchitis to be primary in his case. In the case reported by Dudgeon and Adams the primary lesion was thought to be an epiphysitis of the upper extremity of the radius, in the pus of which influenza bacillus were found. Bertini considered that the meningitis should be regarded as a multiple localization of the infection, since in his case it was uncertain whether the pneu-

[37] Practitioner, 1907, lxxviii, 104.

monia or the meningitis was primary. In Slawyk's case a general infection was found. In a case reported by Mya the lung was thought to be the primary focus, with the occurrence of metastatic foci in a hematoma of the scalp, and an extension of the infection to the meninges through a fracture of the skull. In my case chronic otitis media, along with trauma, was probably the causative agent. The other observers have expressed no opinion in regard to the portal of entry.

AGE AND SEX. The disease greatly predominates among infants and young children. Adults would seem to possess an immunity. Of the cases reported in which the age was noted, 14 (56 per cent.) were under one year of age, 8 between one and ten years, 2 in the second decade, and but 1 beyond this age. Males have been attacked more frequently than females in the cases reported, in which the sex was stated, in the proportion of 16 to 6.

SYMPTOMATOLOGY. The onset of an influenzal meningitis may be sudden without prodromal symptoms, beginning with a chill, high fever, and marked cephalic disturbance. When the base of the brain is first attacked the clinical pictures closely simulates the epidemic type of cerebrospinal meningitis. More frequently the vertex is first involved, giving rise to intense headache without retraction of the head.

In the majority of cases the disease is ushered in with the syndrome of the respiratory type of influenza, headache, rhinitis, bronchitis, general malaise, and fever. Gradually the meningeal symptoms predominate. In infants the onset may be characterized by cough, fever, loss of appetite, and diarrhœa. It is usually impossible to state at what time the involvement of the meninges has taken place. Fraenkel lays stress upon the cramps in the calves of the legs as indicative of a disturbance of the central nervous system. The period of incubation is unknown.

During the initial stage the symptoms differ according to the age and resistance of the patient. The adult complains of severe headache, and of pain in the back of the neck. There may be pain along the entire length of the spine. The patient is usually rational. In infants an early delirium, with marked motor agitation, and extreme prostration is common, and there may be an associated gastro-intestinal disturbance with nausea, vomiting, and diarrhœa. The meningeal symptoms quickly become more pronounced. The head is held retracted by the posterior cervical muscles, and passive movement is painful. If the lesion involves the base of the brain the head may be turned toward the right or left, or paralysis of the facial muscles may result. The child may have convulsive seizures, either general or localized in certain groups of muscles. Muscular tremors in the extremities are common. There is usually marked general muscular rigidity, and the patient lies with the legs flexed on the thighs. A positive Kernig's sign has been present in the majority

of cases reported. The ocular muscles are usually involved, although the eye symptoms are variable. Most frequently there is pupillary dilatation, and strabismus. The pupils may be unequal; they react poorly to light and better to accommodation. The fundi are negative in the majority of cases, although an optic neuritis has been noted in several instances. In our case the disks were found hyperemic and œdematous. Photophobia has been observed. Cutaneous symptoms are not uncommon. A general hyperesthesia may be present. Herpes labialis occurs, but less frequently than in the epidemic form of meningitis. The fever gradually rises to 101° to 104°, and maintains a fastigium; later, in favorable cases, an amphibolous character may develop with morning remissions to normal, and an evening rise of from 2° to 3°. In fatal cases, toward the end, the temperature may become subnormal. A sharp rise of several degrees is not uncommon at any stage of the disease. The pulse rate in infants may be rapid, but bradycardia is not uncommon. In my case the pulse rate never rose above 95, the average rate being 70 to 80 to the minute. On several occasions it was found to be as low as 50. In fatal cases, in the terminal stage, the pulse may become small, rapid, and irregular, with failing circulation. The heart has been found normal on auscultation in all of the observations. The respirations are but slightly affected in the majority of cases. The rate may be somewhat increased. In my case the respirations remained practically normal throughout the course of the disease. In fatal, or severe, cases dyspnœa, at times of Cheyne-Stokes character, has been observed. In the lungs in many cases diffuse rales and patches of bronchopneumonia have been found.

The abdomen is usually found normal, but may be scaphoid, as in the observation of Haedke. Distention and tympanites have been noted. The spleen is sometimes enlarged; more frequently not. Gastro-intestinal symptoms are common, especially nausea and vomiting. Diarrhœa occurs frequently in children. In my case constipation was a marked feature.

The reflexes are variable, sometimes being found normal and at other times exaggerated. The knee kicks and cremasteric reflex was reported as increased in Bertini's case. A positive Babinsky's sign has been found present in the majority of the cases. The abdominal and epigastric reflexes may be absent. Psychic symptoms are usually present and are especially pronounced in children. In adults periods of lucidity alternate with an irrational state. Delirium is common and persistent in young children, and there may be marked motor agitation.

After a few days the symptoms of excitation usually give way to those of depression, and paralysis of various groups of muscles is not uncommon. Macular atrophy and emaciation may be progressive. In fatal cases the patient falls into a state of collapse

with shallow respirations, sometimes showing a Cheyne-Stokes character, the skin becomes clammy, the pulse thready, or imperceptible, and the sphincters relaxed. A subnormal temperature and comatose condition usually precede the fatal issue. In cases in which recovery takes place the improvement is gradual. Convalescence, when once established, is usually rapid and may be complete. In but one of the four cases reported, in which recovery has taken place, was any residue noted: left-sided facial paralysis and a partial right-sided hemiplegia, persisted in a child.

The duration of the disease was usually short. In the fatal cases reported death resulted as early as thirty-six hours, and as late as one month from the onset, the average duration being eleven days. In the cases which have recovered, the illness lasted from eleven days to six weeks.

The blood picture in influenzal meningitis has received insufficient study for any trustworthy conclusions. A slight grade of leukocytosis (13,000) was present in my case, and a differential count showed the polymorphonuclear elements to be somewhat increased. In Adam's case the leukocytes were found to be 10,000 per c.mm.

The urine frequently shows pathological changes. The daily output may be decreased. Retention of urine is commonly encountered. Albuminuria may be present, but is not the rule. A diazo reaction has been noted in some cases.

The complications associated with an influenzal meningitis are many and varied, and most frequently involve some part of the central nervous system. Encephalitis, myelitis, anteropoliomyelitis, optic neuritis, hemiplegia, paraplegia, epidural abscess, acute hydrocephalus, and different paralyses have all been described. In the lungs, bronchitis, bronchopneumonia, and a fibrinous pleuritis are common.

Differential Diagnosis. A positive diagnosis of meningitis due to the influenzal bacilli can only be made by means of a lumbar puncture, and the finding of the organism in the cerebrospinal fluid. In the course of an attack of influenza the patient may frequently show signs of meningitis, which may be in part due to the action of the toxins on the central nervous system, or to the hyperemic condition of the meninges. Associated with this condition are signs of meningeal irritation such as intense headache, vomiting, slow pulse, and a stiffness of the cervical muscles. Such cases occur most frequently in children and may present the full clinical picture of meningitis. There is, however, complete recovery in a few days. To this condition Donath[38] has given the name of "pseudomeningitis grippalis." Some cases have come to autopsy, and at most a hyperemia of the meninges was found, much like meningitis serosa without microörganisms.

[38] Deut. med. Woch., 1902.

It is most difficult, and usually impossible, to distinguish clinically a meningitis of influenzal origin from one due to the meningococcus, or pneumococcus. The symptoms differ according as the vertex or the base of the brain receives the brunt of the attack. Statistics appear to show that the vertex is more frequently affected than the base, and associated with this localization of the process are intense headache, and, but slight, if any, rigidity of the neck muscles. The basal form more closely resembles the epidemic cerebrospinal meningitis. Both may begin with a chill and high fever and stiffness of the neck. In both forms herpes labialis may occur, although usually it is more extensive in the epidemic form. The presence of a preëxisting influenzal attack, with headache, coryza, bronchitis, and fever, or an influenzal pneumonia, makes the diagnosis less difficult. Leichtenstern,[39] in an analysis of cases of epidemic cerebrospinal meningitis, was able to show that such prodromal symptoms are rarely if ever present in the epidemic form.

A secondary pneumonia commonly follows an influenzal meningitis, while such a complication is rare in the meningococcal form. The influenzal origin of the pneumonia may be demonstrated by the finding of influenzal bacilli in the sputum. However, since the majority of cases of influenzal meningitis run their course without respiratory symptoms, an examination of the sputum may give negative results. The co-existence of an epidemic of influenza, or the presence in the patient of a primary focus of influenzal infection in the aural or nasal passages, should lead one to suspect an influenzal process in the meninges. Cutaneous lesions are more common in the cerebrospinal fever than in influenzal meningitis. A petechial rash has been observed in only one case of influenzal origin, and purpura in one other. Bertini states that psychic symptoms are less pronounced in the influenzal form than in the pneumococcal or meningococcal meningitis. The leukocytes may prove to be of assistance in establishing a differential diagnosis. A high grade of leukocytosis of from 25,000 to 40,000 is present in the meningococcal form. The study of the leukocytes in influenzal meningitis has received scant attention. In our case the leukocytes never rose above 13,000, while in another case they were found to be 10,000. It seems probable that a low grade of leukocytosis is characteristic of this disease. The routine taking of blood cultures offers another valuable aid in diagnosis. The meningococcus is commonly found in the blood in cases of epidemic cerebrospinal fever. Blood cultures in influenzal meningitis have so far yielded negative results.

The diagnosis of influenzal meningitis from that of tuberculous meningitis presents no great difficulty, except when the patient is seen late in the course of the disease, when a fully developed stadium meningiticum is established. The onset of tuberculous meningitis

[39] Nothnagel's Spec. Path. u. Therapie, 1896, iv, 123.

is insidious, with a prodromal period characterized by emaciation, asthenia, digestive disturbances, and gradually developing meningeal symptoms. The initial delirium is also wanting and herpes labialis is most uncommon. The presence of tubercles in the chorioid, if found on ophthalmoscopic examination, indicates a tuberculous origin. In very young children the course of tuberculous meningitis may be almost as rapid as that of the influenzal form. In such doubtful cases lumbar puncture affords the only certain means of diagnosis. A cytological study of the cerebrospinal fluid, in a case of tuberculous meningitis, shows invariably an increase in the lymphocytes, while in an influenzal process there is a polymorphonuclear leukocytosis. The tubercle bacilli can also be found in smears. The fluid in tuberculous meningitis is usually clear, while in the influenzal form a turbid or purulent fluid is commonly found.

PROGNOSIS. The prognosis, as in all forms of infectious meningitis, is extremely grave. In influenzal meningitis the infection involves the meninges throughout almost the entire nervous system, and shows a preference for subjects debilitated and infants. Cases occurring in adults are rare. Moreover, Cantani has shown that the central nervous system is a locus minoris resistentiæ for the influenza bacillus. Of the twenty-six cases collected a fatal issue resulted in all but four patients, giving a mortality of 85 per cent. The younger the patient the more grave seems to be the prognosis. Recovery was complete in three of the cases. In the fourth a facial paralysis and partial hemiplegia persisted.

TREATMENT. There is as yet no specific treatment for influenza. The therapeutic indications for influenzal meningitis are those for meningitis in general. The role of lumbar puncture as a therapeutic measure has been much discussed, and the conclusions have been conflicting. For diagnostic purposes lumbar puncture is always indicated. In the majority of the cases the removal of the spinal fluid, which is under increased tension, has been followed by a temporary improvement in the condition of the patient. In Langer's case lumbar puncture was followed by an amelioration of symptoms and a fall in temperature to normal the day following. The child recovered. In Slawyk's case no improvement was noted after puncture except a decrease in tension of the fontanelles. Caccia found that his patient appeared better after puncture. In my case three lumbar punctures were made, following which there was no marked improvement which could be attributed to the removal of the spinal fluid. Even with these apparently conflicting results lumbar puncture seems to afford at present the most rational therapeutic procedure in the treatment of the disease.

ILLUMINATING GAS POISONING.

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Chemistry. The employment of gas manufactured from coal for illuminating purposes is over a century old. The original method was by the destructive distillation of coal or wood in retorts, with subsequent purification. Ammonium and sulphur compounds are the most objectionable impurities of crude gas, and much attention has been given to their removal. The gas-product by this method is principally hydrogen, hydrocarbons, and a very small amount (7 per cent.) carbon monoxide. Toxic qualities of illuminating gas produced in this manner are very low. In recent years the trades, to reduce the cost and simplify the production, have developed new methods of forcing steam through hot coal or coke. The action is not distillation, but oxidation, of coal to carbon monoxide, which is itself reduced by hydrogen. To this "water gas" is added hydrocarbons, that is, methane, ethane, benzene, etc., to fit it for illuminating purposes. The most striking characteristic of "water gas" is its toxicity, due to the excess of carbon monoxide, of which gas it contains 45 per cent., or 38 per cent. more than the carbon monoxide content of coal gas. Carbon monoxide possesses a strong chemical affinity for hemoglobin, with which it combines to form carbon-monoxide-hæmoglobin, resisting decomposition by free oxygen. Hufner states that 1 gram of hemoglobin will take up 1.3 c.c. of carbon monoxide.

Causes. The causes of illuminating gas poisoning are:

1. Hygienic: Deficiency of instruction as to its use, defects of construction of apparatus, and deficiency of ventilation.

2. Psychopathic: Insanities, acute and chronic, exciting absorption of illuminating gas into the blood by inhalation.

Hygienic causes necessarily are responsible for those cases of poisoning which are accidental (non-suicidal), and usually result from lack of instruction of those inexperienced in the manipulation of gas-lighting fixtures. Most cases of poisoning by illuminating gas, however, are the result of suicidal premeditation.

Occurrence. The number of cases of illuminating gas poisoning occurring in large cities has been progressively on the increase in the last ten years. This is certainly the reverse of our expectations, and is a medicosociological question worthy of solution. It cannot be attributed to defects of plumbing, as our buildings are more carefully and intelligently inspected by municipal officers today than they were ten years ago. The use of illuminating gas has been diminishing as electricity succeeds it for lighting purposes.

The enormous increase in the number of cases of poisoning by illuminating gas may be attributed to several changes in the conditions of men: (1) Concentration of population in cities, and (2) increased susceptibility to emotional states and insanity. The enactment of rigid laws restricting the sale of toxic drugs to the layman has also had a tendency toward the increase of poisoning by illuminating gas. The following statistics, while somewhat indefinite, are valuable as an indication of the extent of increase of illuminating gas poisoning:

DEATHS FROM POISONOUS GASES IN NEW YORK CITY.

1867–1880 (twelve years)	16
1880–1892 (twelve years)	202
1889	37
1890	54
1891	64
1902	353
1906	419

PHILADELPHIA.

1899	30
1900	19
1901	26
1902	36
1903	45
1906	50

These are deaths known to be suicidal. In 1906 in Philadelphia 74 deaths from inhalation of poisonous gases were reported in addition to the 50 known to be suicidal. In Boston 43 fatal cases were reported in 1904.

City.	Deaths from inhalations of poisonous gases, 1906.	Suicides by asphyxia, 1906.
San Francisco, Cal.	35	24
Denver, Col	2	3
Washington, D. C.	14	12
Atlanta, Ga.	3	1
Chicago, Ill.	126	55
New Orleans, La.	4	1
Baltimore, Md.	14	9
Boston, Mass.	18	10
Kansas City, Mo.	10	2
Buffalo, N.Y.	5	1
New York, N.Y.	250	169
Cincinnati, Ohio.	6	1
Cleveland, Ohio	6	1
Philadelphia, Pa.	74	50
Pittsburg, Pa.	5	...
Galveston, Tex.	3	...
Norfolk, Va.	3	1
Richmond, Va.	4	...

Comparative studies of these figures from many points of view may be interesting and instructive, but it is not my object to treat of the subject statistically. Having presented the figures, I wish to just-

tify my study of the clinical picture by the progressive increase in death rate. Suffice it to say that in nineteen cities approximately 4000 cases of poisoning from gases, with 582 deaths, have occurred; 340 of the cases were suicidal.

SYMPTOMATOLOGY. The symptoms of gas poisoning are the manifestations of the abolished interchange of oxygen for carbon monoxide in the alveoli of the lungs, and the absence of oxidation of the detritus of cell energy in the body, together with the combination of the constituents of illuminating gases with the physiological elements, changing them into toxic substances. The characteristic features of acute gas narcosis are not constant, and the severity and duration of toxic symptoms depend largely upon the duration of exposure.

Respiratory System. Much has been written of the effect of illuminating gas on the pulmonary system. The respirations are rapid and labored—often of the Cheyne-Stokes type; the face is cyanosed. There is often mouth frothing, the froth frequently containing blood. Most of the fatal cases present, sooner or later, pulmonary œdema as a complication, which is considered the cause of the incident rise in temperature and leukocytosis. I have seen cases in which there was no evidence of pulmonary œdema, with rise in temperature and leukocytosis. W. Gilman Thompson has found œdema, bronchopneumonia, acute congestion, emphysema, pleurisy, and atelectasis at necropsy.

Cardiovascular System. The pulse in all cases is rapid, feeble, and perhaps irregular, being out of all proportion to the temperature and respiration. Examination of the blood shows a most conspicuous change. In a series of cases studied during my incumbency in the Emergency Hospital in 1904 and 1905, I found the red cells reduced 3,000,000 to 1,000,000, and the hemoglobin from 14 per cent. to 69 per cent., the degree of reduction being inversely proportional to the duration of exposure and severity of symptoms, The leukocytes were increased, varying between 9000 and 22,000. Morphologically, the red blood cells showed marked poikilocytosis, granular and hydropic degeneration, polychromatophilia, and enucleation. Polychromatophilia is especially conspicuous, and would seem to confirm Engel's theory, that these cells appear when rapid new formation of red corpuscles is demanded and when there is not time for complete shrinkage of nucleus and development of orthochromatic cells. The color index was minus, and the specific gravity and coagulability increased. Thompson reports an increase in red blood cells, but my study of 15 cases, herewith appended, fails to corroborate his observations except in the early stages (two to six hours), when the red cells and hemoglobin were usually normal or slightly increased. The anemia was, in favorable cases, followed by a return to normal; but in fatal cases the anemia persisted or increased. While there was a marked change in the hemocytic

elements, probably due to effects of carbon monoxide, I am of the opinion that the primary increase in red blood cells and leukocytes is in a large measure due to the transudation of blood serum from the vessel walls into the tissues. The whole blood is increased in specific gravity and coagulability, with the presence of non-inflammatory œdema of the lungs, cutaneous blebs, and often serous leptomeningitis. The polycythemia, if due to a decrease in the volume of the plasma, is only a relative polycythemia, and the concentration of solid elements of the blood only temporary. Much importance was attached to the primary increase in red cells per cubic millimeter during the early stages, and the phenomenal decrease after a few hours. The pronounced secondary anemia occurring within five or six hours after the onset of coma is in a degree due to the fact that most of these cases are submitted to venesection and intravenous transfusion of $\frac{N}{10}$ saline solution, which produces hydremia and low red cell count. The presence of abnormal morphology, with slow return to normal is in favor of hemolytic anemia. The blood pressure is at first increased, but after prolonged exposure rapidly diminishes.

Exposure.	Coma.	Temperature.		Pulse.	Respiration.	Blood findings.		
		Maximum.	Minimum.			Leukocytes.	Red blood corpuscles.	Hemoglobin.
1. 2 hours	3 hours	100°	98°	112	30	10,000	5,000,000	80%
2. 3 hours	5 hours	101°	98.4°	118	30	No rep't		
3. 2 hours	1 hour	100°	98.2°	126	28	No rep't		
4. 3 hours	9 hours	100.4°	98°	126	30	12,000	4,600,000	70%
5. ½ hour	None	99.4°	98°	100	24	9,000	4,000,000	80%
6. 5 hours	72 hours	108°	100.8°	160	68	18,000	3,000,000	20%
7. 8 hours	12 hours	105°	96.8°	140	48	No rep't		
8. 3 hours	10 hours	100.8°	98°	120	32	No rep't		
9. 6 hours	24 hours	106.6°	103.2°	140	48	No rep't		
10. Unknown	38 hours	108°	98.2°	164	66	22,000	4,200,000	30%
11. 6 hours	60 hours	101°	97.4°	132	62	No rep't		
12. 4 hours	16 hours	103°	99°	112	40	13,800	.....	66%
13. Unknown	4 hours	99°	97.8°	100	22	No rep't		
14. 4 hours	12 hours	99.2°	97°	100	26	12,300	4,612,000	49%
15. Unknown	18 hours	100.4°	97°	100	40	15,000	4,200,000	50%

Nervous System. Coma is prompt after short exposure to illuminating gas. The reflexes are usually completely abolished. The pupils are usually contracted and do not react, but may be dilated, normal, irregular, or respond to light. Temporary nystagmus is common. Muscular twitchings may precede or follow coma.

Most cases present incontinence of the sphincters. Delirium is a usual complication. Hemetson reports a case with convulsions lasting nine days. Among diseases of the nervous system following gas poisoning, the following have been reported: hemiplegia, dementia, acute mania, serous leptomeningitis, disseminated encephalitis, multiple sclerosis, and multiple neuritis.

Urinary System. The urinary findings are for the most part negative. In three of my cases the urine showed evidence of an acute hemorrhagic nephritis.

Skin. The skin is usually cyanosed, cold, and dry. I wish to call attention especially to the appearance of blebs on the extremities and back, usually occurring in chains, in cases in which the coma persists for twelve hours or longer. These bullæ contain clear serum, and have frequently been mistaken for the effects of excessive external heat applied in treatment. They were present in five cases, all of which ended fatally.

Temperature. The temperature is usually subnormal during the first twelve hours, and reaction is characterized by a rapid rise, varying from 99° to 103° F. The temperature returns as rapidly to normal as it reached the fastigium.

Vagaries of temperature are due to: Disturbances of normal chemical processes, disturbance of circulatory equilibrium, or altered pulse and respiration.

In cases in which exposure has been prolonged, and in which coma is consequently deep, the temperature rises rapidly, reaching 104° to 110° F. These cases terminate fatally within twenty-four to seventy-two hours. The rise in temperature is usually coincident with the development of œdema, but I do not agree that the sudden development of high fever is caused by the pulmonary condition, but rather incline to the view that it is the result of overwhelming toxemia, the œdema being of hemolytic origin.

Diagnosis. The history of the case is sufficient to make the physician reasonably certain of the diagnosis, but the fact that a patient is found in coma in a room stifling with the odors of illuminating gas without any mode of free entrance of atmospheric air should not be sufficient to forego a careful examination for evidence of other toxic substances introduced by the suicide to make the termination certain. At least a small percentage of the cases of illuminating gas poisoning are complicated by the effects of toxic doses of other poisons capable of producing death.

Prognosis. The prognosis should be based upon a careful and intelligent consideration of the following facts: Duration of exposure; degree of coma; condition of the pulse, respiration, and temperature; condition of lungs; condition of the blood; and the presence of cutaneous blebs. If the exposure be long, the coma is correspondingly deepened and more prolonged. Coma for forty-eight or more hours augurs unfavorably. The onset and rapid

development of œdema with pronounced hemolytic changes is unfavorable. The persistence of anemia and coma with the onset of trophic changes should be looked upon as indicating a most doubtful result. Short exposure to illuminating gas is followed by prompt response to treatment, with recovery. All the cases which develop cutaneous blebs end fatally.

The cause of death is not, in all cases, asphyxia. The leukocytosis, hemolysis, frequency of complications involving the nervous system, and constant pathological changes in the brain and spinal cord, strongly indicate toxemia.

PATHOLOGY. Little was known of the morbid anatomy until the investigations of Thompson in 1904. The most marked changes are found in the blood. The kidneys frequently show evidences of acute nephritis of the glomerular type, and many of the patients who live for twenty-four hours or more undoubtedly succumb to an intercurrent uremia. The lungs may show no changes whatever; however, œdema, acute congestion, and emphysema are common in the cases coming to autopsy. Changes in the brain and spinal cord are by far the most constant pathological findings. Parenchymatous neuritis, multiple sclerosis, serous leptomeningitis, encephalomyelitis, and cerebral hemorrhage have been reported.

TREATMENT. The management of patients suffering from intoxication by illuminating gas has been unsatisfactory, because of the affinity of CO for hemoglobin, and lack of knowledge of the pathological and metabolic processes which the intoxication produces. Inhalation of oxygen has always been unjustly esteemed in the treatment. The use of oxygen by inhalation is of doubtful efficacy, since it seems improbable that the excess of oxygen over that in normal atmosphere can become physiologically combined with the hemoglobin in exchange for carbon products.

The patient should be taken from the room and into fresh air. The tongue should be retracted from the mouth and so retained by means of a hemostat, improvised gag, or tongue retractor. If necessary, artificial respiration should be begun at once. The patient should be removed without delay to an institution or physician's office, where immediate phlebotomy should be performed. A pint to a pint and a half of blood should be removed, and simultaneously a quart of $\frac{N}{10}$ saline solution transfused in the median basilic or cephalic vein of the opposite forearm. Venesection can be repeated two hours after the first bloodletting, if the patient be not doing well. Saline solution should be given subcutaneously every two hours in quantities of one pint, or by the rectum continuously. Saline solution diminishes toxemia, lessens the tendency to œdema of the lungs, increases the affinity of red cells for oxygen, and stimulates the circulatory system. At the outset the patient should be given by hypodermic injection ether, 30 minims, atropine, $\frac{1}{100}$ grain, and

suprarenalin, 30 minims. Nitroglycerin and vasodilators in general should be avoided. Suprarenalin is administered on a rational basis, presuming the œdema, etc., to be the result of increased capillary permeability. The patient should be protected from exposure by an abundance of blankets. External heat should be applied (bearing in mind that the skin is especially susceptible to heat).

While venesection and intravenous injection of saline solution are being done, an assistant should proceed to wash the stomach thoroughly with a solution of potassium permanganate, and follow lavage by the introduction of magnesium sulphate (3 ounces). The respiration and pulse should be watched closely, and stimulated carefully as indicated. Urinalysis should be made daily.

Crile has advocated direct transfusion of blood, and has recently reported results of animal experiments, but his statistics do not show a greater percentage of recoveries than do the active stimulation, venesection, and intravenous injection of saline solution.

Deductions. Death from gas poisoning is rapidly on the increase; changes in the blood are conspicuous and severe; toxemia is pronounced; the severity of the symptoms and the duration of the coma depend upon the duration of the exposure; complications of the nervous system are common; cutaneous vesicles appear frequently in severe cases; elevations of temperature occur independently of œdema; poisoning by illuminating gas is sometimes complicated by toxic symptoms of other poisons; saline solution diminishes œdema of the lungs; oxygen is useless; direct transfusion is impracticable; asphyxia is not often the cause of death; the bloodvessels are dilated; the tendency to exudation of serum is increased; suprarenalin in repeated doses is indicated.

CIRCUMSCRIBED SEROUS SPINAL MENINGITIS.[1]

A LITTLE-RECOGNIZED CONDITION AMENABLE TO SURGICAL TREATMENT.

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A collection of clear fluid in a cyst of the spinal pia-arachnoid is a condition little known in America, as only one case occurring in this country is on record (Spiller, Musser, and Martin,

[1] Read at a meeting of the College of Physicians of Philadelphia, December 2, 1908.

1903), and only a few are to be found in the German literature. So far, the French and English journals contain no examples. A recent excellent *resume* of the subject by S. Adler makes a complete critical digest by me unnecessary, and yet, because of the little attention paid to the condition, it has seemed desirable to bring the subject before the College.

Almost nothing is known as to the origin of apparently idiopathic collections of fluid within the pia-arachnoid. The fluid may be from the bloodvessels of the pia, as has been suggested, and the mesh-like structure of the leptomeninges may predispose to adhesions, but why these cysts occur in any given case, especially where there are no evidences of inflammation, we do not know. The symptoms are those of circumscribed compression of the spinal cord, and the condition cannot be distinguished clinically from tumor of the cord. It is of great importance, as operation is easy and cure seems to be permanent in typical cases.

In the report of the case of Mendel and Adler, in which an operation was performed by the latter, it is stated that the much-swollen arachnoid protruded through the dura at the operation and appeared violet-blue in color, apparently exactly as in the case we reported. The arachnoid was punctured, and about a teaspoonful and a half of clear fluid escaped in a strong stream and was lost in the bandages. The intra-arachnoidal cavity in which the fluid had been contained was found closed at all parts by adhesions. The improvement after this operation was very marked.

Krause and Oppenheim made their first report of this condition in 1906, but they did not refer to previous work on the subject. This was not extensive, and consisted of the reports of three cases (Schlesinger, Schwartz, and Spiller, Musser, and Martin[2]). Schlesinger, in his well-known monograph on spinal tumors, gave the history of a case in which a cyst of this character was found at necropsy. Schwarz's case (1897) was one with the symptoms of syphilitic spinal meningitis, and after death intense meningomyelitis was found, with a meningeal cyst. This seems to have been a case different from the typical examples, in that closure of a space within the pia-arachnoid might easily occur from the intense meningeal inflammation. Neither of these cases was with operation. The first case reported anywhere with operation was the case by Spiller, Musser, and Martin.

In that case a delicate pial cyst was found and evacuated by Dr. Edward Martin. The operation was on June 30, 1902. The patient had suffered intensely. She has been reëxamined by Dr. Musser and me within the past few weeks, and she has now no symptoms of her former trouble except slight pain in one buttock when she presses over the scar made by the operation. She has gained much in weight and is in excellent health.

[2] Univ. Penna. Med. Bull., March and April, 1903.

This is not only the first case with operation, but is the only one on record in which recovery has persisted after operation so long as six years and five months.

Krause, in operating on 22 cases of spinal compression, expecting to find tumor, found circumscribed serous meningitis in six, although it is not certain that this was the only lesion. Adler remarks that the condition is not a scientific curiosity, as some may think, but is of practical significance. He refers to a case seen by Stroebe. A very similar condition on the under surface of one cerebellar lobe has been described by Placzek and Krause.

The associated lesions that have been found are: Necrotic osteitis of the vertebræ with pachymeningitis (Krause); scar-like adhesions between the dura and pia, probably with spinal gliosis (Krause); bony projection on the inner surface of a vertebra (Krause); and meningomyelitis (Schlesinger, Schwarz).

As Adler remarks, no cause was found in the case reported by him with Mendel, nor in one case of Krause, nor in the case of Bruns, nor in our case. Adler is inclined to believe that in the case reported by himself and Mendel tuberculosis may have been present, as the patient had had pulmonary tuberculosis; and he hesitates, on the basis of four cases, to speak of an idiopathic form of circumscribed serous meningitis. He suggests the possibility of spinal puncture, and refers to the fact that after operation the fluid does not seem to collect again. Bruns, stimulated by Mendel and Adler's[3] paper, publishes his case more in detail, and reports almost complete recovery two years after the operation.

A case reported by W. C. Krauss hardly belongs to this group of cases, as the cyst was not confined to the pia-arachnoid. The diagnosis of spinal tumor was made, but an extradural cyst in eroded vertebræ was found. Dr. Roswell Park states, however: "It seemed evident that there was a cavity with eroded walls connecting with the spinal canal, containing mostly fluid, with a little semi-solid tissue material."

It is questionable whether the spinal cyst described by Schmidt should be included under this type. It was intradural, but not a cyst of the pia. Its wall had the consistency of the dura.

Although the literature on circumscribed serous spinal meningitis, as shown by this *resume*, is meagre, it is sufficient to stimulate us to pay attention to the condition and to encourage us in the belief that certain cases with the symptoms of spinal tumor may be more amenable to surgical intervention than are many tumors.

[3] Berl. klin. Woch., August 31, 1908. The literature is given in this paper; Bruns, ibid., September 28, 1908; Krauss, Brain, 1907, xxx, 533; Schmidt, Deut. Zeitsch. f. Nervenheilkunde, 1904, xxvi, 318.

VARIX OF A PAPILLA OF THE KIDNEY A CAUSE OF PERSISTENT HEMATURIA.

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During the last few years the attention of genito-urinary surgeons has been attracted to the more obscure forms of hematuria by the reporting of a large number of cases in which no sufficient cause for bleeding was made out, in some cases even after the kidney had been removed. The classification of these cases is still chaotic and unsatisfactory.

In 1898 Mr. Hurry Fenwick reported a case of papillectomy for intermittent hematuria of five years' duration, in which the pathologist reported varicose veins in the mucous membrane covering the papilla. Since that time he has reported five cases of a somewhat similar nature in which the lesion appeared to be changes in the venous blood supply about the papillæ.

As far as I am aware no similar cases have been reported in this country. The following is a case of this apparently unusual condition:

Mr. A. B. S., aged fifty years, entered the Massachusetts General Hospital, September 27, 1907, in the service of Dr. Maurice H. Richardson, through whose courtesy I am enabled to report the case.

Thirty years ago he strained his back lifting, and immediately afterward passed what was thought to be bloody urine. From time to time since, often at considerable intervals, he has passed blood without any subjective symptoms, and has given the matter little thought. Seven months ago hematuria returned and the urine has since been bloody about one-third of the time. Five weeks ago he had sudden sharp pain in the left side about the level of the iliac crest. The pain lasted three hours, was colicky in character, tended to shoot upward and inward, and was accompanied by vomiting. There was no pain on micturition. Urine was voided two to four times a day, and three or four times at night. This is a slight increase in nocturnal frequency over previous years. This attack led his physician, Dr. E. T. Drake, of Franklin, New Hampshire, to regard the case as one of stone in the ureter.

The patient was a fairly well-developed, anemic, somewhat cachectic man. The heart sounds were regular, somewhat distant; there was no murmur, no enlargement of the heart, and the chest was otherwise normal. The abdominal examination was negative. The left inguinal glands were slightly enlarged. Rectal examination showed the prostate to be normal.

On September 27, examination of the blood revealed the hemo-

globin, 70 per cent., the leukocytes 5000. A differential count was as follows: Neutrophiles, 60 per cent.; lymphocytes, 38 per cent.; and eosinophiles, 2 per cent. One normoblast was found.

On September 27, the urine was bloody in color, acid in reaction, contained a slight trace of albumin, but no sugar. The sediment was made up largely of fresh and degenerated blood corpuscles, leukocytes, and a little free fat. From this time until October 5 the urine remained practically the same. Cystoscopic examination showed a normal bladder, and blood in considerable amount coming from the left ureter, the orifice of which was normal.

The condition of the patient was such as clearly to require relief, as his anemia showed no improvement and tended to increase; *x*-ray examination was negative.

Operation was done October 5 by Dr. M. H. Richardson. The kidney was exposed through an oblique incision on the left side, running from the tip of the twelfth rib downward and forward. An apparently normal kidney was delivered without difficulty. Palpation of the kidney and the upper portion of the ureter failed to show anything abnormal. The patient's condition was such that a nephrotomy with its attendant possibilities of bleeding seemed to Dr. Richardson unwise, in which opinion I entirely concurred. The choice, therefore, appeared to lie between decapsulation and nephrectomy. The latter operation was decided upon and done without difficulty. The patient stood the operation well. Upon the following day he passed a good amount of urine, although it was still markedly blood stained. Two days after the operation the urine was clear and remained so up to the time of discharge from the hospital, two weeks later. On April 25, 1908, the patient reported by letter that he has been entirely well since the operation and steadily at work. The twenty-four-hour amount of urine on April 28, 1908, was twenty-seven ounces; it was free from albumin.

The kidney was submitted to Dr. William F. Whitney, who has recently reported his observation to the Obstetrical Society as follows: "I examined it at once, and in general it appeared as a somewhat pale but otherwise normal kidney. On closer inspection it was noticed that the tips of one or two of the papillæ at one end of it were reddened and a little spongy. These were cut out at once carefully and hardened in Zenker's fluid, embedded in paraffin, sectioned, mounted, and stained with eosin and methylene blue. The microscopic examination showed the small venules at the tip of the papilla dilated irregularly to twice or three times their normal size, and covered on their free surface with the finest possible film of connective tissue and a single layer of epithelial cells. Here and there they projected as varicose knuckles above the surface (Figs. 1 and 2). The conditions, in fact, were such that the slightest violence must have caused a rupture with subsequent escape of blood. In one specimen a rent was found in one of these thin-walled channels,

but it cannot be stated positively that it may not have been an artifact. The lumen of the vessels, in many places, was filled with a finely granular detritus and occasional blood corpuscles, but no

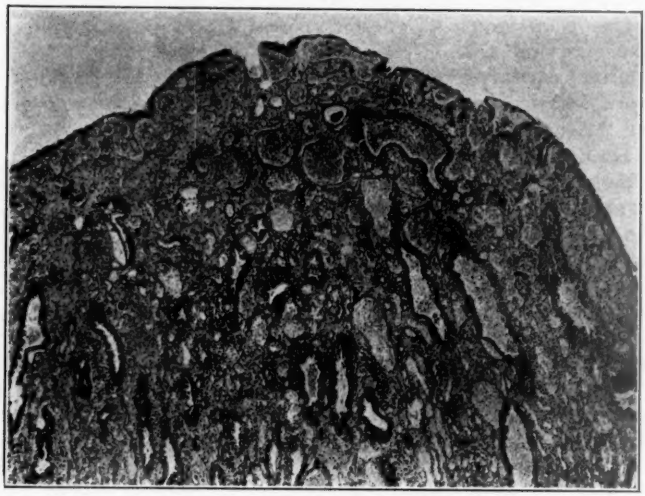

FIG. 1

FIG. 2
Dilated venules at the tip of a renal papilla.

well-marked thrombi were seen. That the hemorrhage must have taken place here, however, is borne out by the fact that the straight tubules of this region contained blood corpuscles, which were not found higher than the base of the pyramids. The anatomical conditions described are certainly adequate to cause frequent and severe hemorrhage, for we have only to call to mind what an insignificant lesion will produce a very severe epistaxis to realize what might happen after the rupture of one of these small varicose vessels. It is interesting to find what an abundant vascular plexus there is at the apex of the normal papilla, and by what thin tissue the vessels are separated from the external surface. The size of the normal vessels, however, is very much less than in this case, so that their covering is actually and relatively very much thicker. It is only to be wondered at that hemorrhage is not much more frequent from this source, and it possibly may be and may account for blood found in the urine in some cases of congestion of the kidney."

The only other similar cases are the six of Mr. Fenwick's[1] above referred to, which are here briefly summarized:

Case I.—March, 1898, female, aged eighteen years. Intermittent hematuria for five years. Papillectomy. On examining under water it was not villous as was supposed, but the vessels of the mucous membrane clothing the papilla were markedly varicose. Mr. Targett reported there was no evidence of growth, but there was congestion of the vessels with extravasation of blood and an increase in the cellular stroma. This might be an early stage of a fibrous condition such as is not uncommon at the tips of the papillæ.

Case II.—September, 1899. A female with profuse hemorrhage two weeks before without any other symptoms. At operation a bright-red varicosed condition, similar to that which had been encountered in the first case, was seen. Papillectomy. Mr. Targett reported the vessels in this part of the kidney distended with blood, and some extravasations.

Case III.—July, 1902, male, aged thirty-six years. Hematuria on slightest exertion. Pelvis opened and blood seen to issue from lower infundibulum. Sulphate of iron applied; no benefit. Nephrectomy two months later. Kidney was found in a state of subacute nephritis, possibly the result of first operation. Regards it as primarily an angiomatous papilla.

Case IV.—Male. Hematuria for eight weeks. Operation consisted of an incision into the cortex of the lower third without entering the pelvis. Bleeding disappeared after a few days and healed rapidly. No return at the end of six months.

Case V.—April, 1898, male, aged thirty-eight years. Ten days previous symptomless hematuria. Cystoscopy: bloody efflux from left ureter. Operation: The finger was inserted into the pelvis

[1] Clinical Cystoscopy, London, 1904, p. 392.

through a deep incision in the cortex of the lower third. Hemorrhage ceased and had not returned after a year.

CASE VI.—September, 1902, female, aged forty years. Had dark blood in her urine for two years continuously without symptoms. Operation: A deep incision made in the convexity of the cortex of the lower third. Hemorrhage persisted. Two months later nephrectomy. On dissection a dark purple papilla appeared and oozing from a bright point in the apex was a little blood. Mr. Targett reported that the cortical tissues appeared quite healthy both as regards the glandular tubules and the glomeruli, but on passing up the papilla toward the pelvis of the kidney was found an extensive dilatation of the small vessels running up the papilla. Indeed, the condition was so marked at the summit of the papilla that it constituted a capillary nevus or angioma, and many of the larger vascular channels were distended with clots. In consequence of this growth of vessels the papilla was greatly enlarged and the covering of transitional epithelium was greatly thinned or actually wanting at the apex. The capillary vessels must, therefore, have been placed in direct communication with the cavity of the pelvis of the kidney.

TREATMENT. For most cases of this condition it seems that nephrectomy is an unduly radical operation, although in the present instance it was amply justified. Decapsulation and nephrotomy are likely to be valueless, because they fail to attack the essential lesion, and if they give any benefit it is because the general congestion is diminished. Mr. Fenwick has had some success with the somewhat blind destruction of the papilla, through a short incision in the cortex, but the method is somewhat less accurate than the condition requires for satisfactory treatment.

Since in practically all of these cases it is possible to deliver the kidney so that the pelvis is readily accessible, it is at least possible that a free incision into the pelvis and exploratory pyelotomy would enable the lesion to be dealt with under direct vision. If the spongy tissue can actually be seen it would not be difficult to destroy the superficial vessels with a properly constructed electrocautery. There is, I believe, every reason to expect that future investigation will show this condition to be a not uncommon cause of hematuria, and one which can be dealt with without sacrificing the kidney.

THE PROBLEM OF IMMUNITY IN TUBERCULOSIS.[1]

By Edward R. Baldwin, M.D.,
of Saranac Lake, New York.

It is my purpose to take a brief retrospect of past achievements in attempts artificially to protect against tuberculosis, and then to indicate what seems to me the special problems for the future. It must be confessed that much discouragement has resulted from the numerous experiments on animals in this direction during the past two decades. This problem has engaged the thought and labor of the foremost workers in immunity research, and it will continue to do so with the enthusiastic hope inspired by every new discovery, however little it may contribute to the ultimate object.

A review of the achievements already attained, with due credit to the authors for priority, is peculiarly difficult, and also impossible in the limits of this address. The difficulties are real because of the simultaneous experimentation in different laboratories and countries, which have independently followed similar lines impelled by the same ideas. The most important example of this common *motif* is the principle of immunization with bacteria of attenuated virulence, formulated by the immortal Pasteur and applied to tuberculosis as soon as the illustrious Koch made it possible by the discovery of the bacillus. It is noteworthy that this principle holds at present the leading place in the hope for success in the future, and it is natural that these experiments should have begun in France (Daremberg, Grancher and Ledoux-Lebard, Martin, Hericourt and Richet, and Courmont and Dor). The immediate results were discouraging; too little was known of the mechanism of immunity to make use of the crude methods then employed as a basis for thorough experimentation; and the discovery of tuberculin and antitoxins for other diseases directed attention to these fields of greater promise.

As it is not generally known that Americans engaged in the earlier experimentation with a considerable degree of success, it is appropriate that they should receive mention here. As early as 1889 Dixon made some preliminary experiments with attenuated bacilli, and Trudeau, working under exceptionally difficult conditions, produced a relatively strong immunity with cultures of avian tubercle bacilli (1892), and later with attenuated human cultures. The late Emil de Schweinitz, in 1894, had more marked success on guinea-pigs immunized with the same attenuated cultures employed in Trudeau's experiments. This period was also one of diligent but unsuccessful search for antitoxic immunity by means of divers extracts and products of the tubercle bacillus. The soluble extracts of tubercle bacilli having failed to immunize

[1] Read at the International Congress on Tuberculosis, Washington, D. C., October 1, 1908.

animals, Koch introduced the emulsions or new tuberculins, "T. R." and "B. E.," which were in some degree protective against infection.

Experiments with pseudotubercle bacilli and mammalian types, supposedly altered by passage through reptilians, also promised fruitful results, but they have not fulfilled this hope up to the present time.

The discovery by Theobald Smith, in 1895, of differences in form and virulence between bacilli from bovine and human sources, was another valuable contribution destined to influence the course of immunity experimentation on cattle. Pearson and Gilliland in America were among the first to attain a high degree of immunity in cattle by the use of the human type of bacilli, following up their first work by an extensive series of practical tests.

During the past decade many workers have turned to the study of immunity against tuberculosis in cattle. Von Behring and Koch with their associates have introduced methods of immunization for cattle, the basis of which was the intravenous inoculation of living human cultures. The "bovovaccin" of von Behring consisted of dried human cultures designed to be twice inoculated within an interval of three months. The "tauruman" of Koch and Schütz was an emulsion of more virulent human type for a single protective inoculation. Coincidently, Pearson and Gilliland succeeded equally well with successive inoculations during shorter intervals. Besides these methods von Baumgarten employed subcutaneous inoculations with good results, Calmette and Guèrin used the gastro-intestinal route by feeding the protective virus, and Heymanns enclosed virulent bacilli in capsules which were introduced subcutaneously for immunization without resulting danger of infection. Klimmer, of Dresden, claims excellent results from the subcutaneous injection of a virulent and modified human bacilli supposed to be passed through lizards.

The world-wide interest created by von Behring's announcement, in 1902, of a practicable method of immunizing calves, led to the hope that this aspect of the problem had been solved. An enduring immunity for cattle with no danger associated with it was an alluring prospect, and extensive experiments were at once undertaken. The outcome of these has been less satisfactory than was hoped for. A high degree of resistance can be conferred by various methods of inoculation with human and attenuated bovine bacilli for a period varying from six months to two years. Unfortunately, exposure to natural infection or to inoculation with bovine virus after this period has resulted disastrously. Some of the animals completely lose their immunity and others retain but little of it. The situation is, therefore, at present not encouraging for the establishment of a long-continued immunity by any method, either in cattle or men.

Moreover, the use of living virulent bacilli as a bovine vaccine, either intravenously or subcutaneously, cannot be regarded as safe,

since they have been discovered in the subcutaneous abscesses and milk at least nineteen months after the protective inoculation (Schroeder and Cotton, and Weber and Titze). The trend of experimentation has naturally been toward the use of bacilli either deprived of reproductive power or modified by conditions of growth so as to lose parasitic features. The possibility of a strong relative immunity has been demonstrated, but much yet remains to be accomplished to make it useful.

To overcome the objections due to the use of living human bacilli in cattle, and to apply the principle of immunization to mankind, have been the problems of recent years. Hope of this achievement was held out by von Behring at the last International Congress at Paris in 1905. Nothing definite has been made public since to indicate that this hope was justified or that the immunizing and therapeutic properties of the so-called "tulase" were superior to the bacillary preparation T. R. of Koch, introduced a decade before.

One fact has been prominent in the course of all investigations, and that is the superiority of living bacilli over all the preparations of dead bacilli for protective inoculation. The vital element has a more pronounced influence, even upon animals which completely resist infection by the immunizing vaccine and show no trace of the inoculated bacilli a short time afterward in their tissues. It is natural to suppose that the bacilli perish too quickly to adjust themselves to a parasitic existence by producing any hypothetical secretion, which might be the secret of their greater protective influence. It is admitted, however, that the degree of immunity is directly proportional to the virulence of the vaccine. The subtle difference between the immunizing value of living and of dead bacilli needs more investigation; likewise also the cause of variations in virulence.

Repeated protective treatment must be considered necessary for success from the present outlook, and by means of an agent equally innocuous to cattle and mankind. It has been found that a period of two months after the first immunizing dose is required to develop the specific resistance in calves. Obviously, they must be protected from exposure to infection during this period. Probably the subsequent protective treatments will more quickly become effective.

It appears desirable to establish as strong local resistance as possible by subjecting all avenues of infection to local immunization; for example, by feeding and inhalation of the vaccine.

In order to adjust the dosage and intervals the finer mechanism of immunity must be closely studied. The agglutinin and opsonin tests have not been satisfactory measures of resistance, and some way of estimating specific latent antituberculous cell energy is needed. When natural infection is taking place or the individual is undergoing immunization there are, it is true, evidences of

changes in the blood, but when no such stimulus is active the content of antibodies—agglutinin, opsonin, or lysin—slowly drops to a normal level. There is then no sign of the latent specificity which we are as yet able to recognize, although a renewed infection or a tuberculin test may elicit it.

Another phase of the problem is to establish a correct balance between the specific response to infection, which occurs during the hypersensitive stage of immunity and the ability of the tissue cells to assimilate the poisons without harm.

An immunity that tends only to arrest the infection but not to overcome it, is not wholly beneficial when it creates ulceration at the portal of entrance of the bacillus (Th. Smith). Hence the question whether hypersensitiveness artificially induced by protective inoculations is beneficent or otherwise must be considered. It would seem vastly better, from what we know of the effects of hypersensitiveness in heightening the affinity of the body cells to a harmful degree for the poisons of tubercle bacilli, that it should be avoided. Specific bacteriolytic powers are useful in combating bacteria, but not in assimilating the dead and digested body substances of bacteria.

Fortunately the number of bacilli to be disposed of at any given time is small under natural conditions of infection. It is conceivable that a relative tuberculosis immunity without tuberculin susceptibility being produced at some time during its development might be defective. On the other hand, complete tolerance to tuberculin in cattle may be associated with a high degree of resistance to infection.

The problem, therefore, seems to be to create tolerance for the bacillus poisons and its products which have resulted from lysis, or to aid their safe assimilation by the tissues.

Without the unknown quality called "tolerance" no real immunity can exist, and the earlier in life this can be established with absolute safety the more resistant the adult must become. That there is danger of harm in the process may easily be surmised from the grave impairment of nutrition resulting from experiments with dead bacilli, and the well-known anemia accompanying so-called latent tuberculosis. These difficulties I conceive to be the prominent ones, but they are here treated in a confessedly superficial manner.

The studies of Bartel on the influence of lymphatic cells upon the tubercle bacillus, as well as those of Opie on the leukocytes, promise to enlarge our knowledge of this subject. Still more light may come from investigations now in progress on the mechanism of anaphylaxis and its prevention.

Finally the problem of passive immunity is still a distant goal which should not be forgotten. It must not be thought hopeless considering the progress of biologic research, though a serum therapy furnishes but a faint probability of success. Some other method of

directly neutralizing the cell poisons may yet be discovered with the increasing facilities generously being devoted to medical research. On this rests the hope of an efficient therapy to supplement all other means of prevention and cure.

THE CAMMIDGE REACTION IN EXPERIMENTAL PANCREATITIS.[1]

By JOHN SPEESE, M.D., AND EDWARD H. GOODMAN, M.D.,
OF PHILADELPHIA.

(A preliminary report, from the William Pepper Clinical Laboratory of the University of Pennsylvania and the Private Laboratory of Dr. John H. Musser, Philadelphia.)

IT is rather surprising that, despite the great clinical value claimed for his test, Cammidge[2] has so far made no attempt to control his observations by experimental work. Eichler[3] studied the effect of experimental pancreatitis on the urine, producing in one dog hemorrhagic pancreatitis, and in two dogs a diffuse purulent pancreatitis. The urines of these dogs before operation were negative, confirming the observation previously made that the urine of normal men, dogs, and rabbits does not give a positive pancreatic reaction. The post-operative examination of the urine, in each instance, was positive, which led Eichler to conclude that the test is of great value in diagnosticating pancreatic disease. As he used the *A* and *B* reactions in his studies, and as these reactions have been severely criticised by Ham and Cleland,[4] Schroeder,[5] Gruner,[6] Wilcox,[7] and Haldane,[8] the the value of Eichler's conclusions may be questioned.

In 1907 Cammidge[9] described a third, or *C* reaction, which he claimed does away with many objections raised by his critics. Very little clinical work has been done with the *C* test, apart from Cammidge's own researches, and, so far, no experimental work has been reported. The papers of Cammidge, Schroeder,[10] and Goodman[11] have presented so much clinical evidence in favor of the reactions that we deemed it advisable to control these observations by experimentation.

[1] Read at a meeting of the College of Physicians of Philadelphia, December 2, 1908.
[2] Robson and Cammidge, The Pancreas: Its Surgery and Pathology, 1908.
[3] Berl. klin. Woch., 1907, p. 769.
[4] Australasian Medical Gazette, 1904, p. 399; Lancet, 1904, i, 1378.
[5] Amer. Med., 1904, p. 406.
[6] Lancet, 1904, i, 1459.
[7] Lancet, 1904, ii, 211.
[8] Edin. Med. Jour., 1906, xx, 418.
[9] Loc. cit., p. 252.
[10] Jour. Amer. Med. Assoc., 1908, li, 837.
[11] Read by invitation at a meeting of the Philadelphia Academy of Surgery, November 2, 1908, and to be published in the Annals of Surgery, February, 1909.

During a study of experimental pancreatitis conducted by Sailer and Speese,[12] the examination of the urine for the Cammidge reaction was productive of such interesting results that we were led to a systematic study of this phase of the question.

In five dogs 10 to 30 c.c. of cottonseed oil was injected into the pancreatic duct, a procedure which causes rapid necrosis of the pancreas. In three of these cases, studies were made of the urine before and after operation, and in two cases the examination before operation was omitted. The dogs were killed eight hours after the operation.

CASE I.—The urine before operation was not examined. The urine after operation gave a positive reaction. Macroscopic examination of the pancreas showed a diffuse necrotic process which involved most of the organ. The microscopic study revealed complete destruction of the tissue.

CASE II.—The urine before operation was negative; the urine after operation was negative. The pathological examination of the pancreas showed neither macroscopic nor microscopic lesions. In this case pancreatitis was not produced, owing to the attempt to inject oil into the pancreatic duct being unsuccessful.

CASE III.—The urine before operation was not examined; the urine after operation gave a positive reaction. The postmortem examination of the pancreas showed a diffuse necrotic process; lesions similar in nature were seen microscopically.

CASE IV.—The urine before operation was negative; the urine after operation gave a positive reaction. The macroscopic and microscopic study of the pancreas showed a diffuse necrotic process.

CASE V.—The urine before operation was negative; the urine the first hour after operation was negative; the urine the fourth hour after operation gave a positive reaction. The usual necrotic appearance following oil injections was seen; the microscopic examination failed to reveal any normal structure except in the tail of the pancreas. The animal in this case was killed four hours after operation.

Encouraged by these results, we thought it of interest to study the urine in cases of non-acute pancreatitis. Ligation of the pancreatic duct seemed to be the simplest method of producing such a lesion. The plan which we adopted in three instances was to examine the urine before ligation of the duct, and at the end of each twenty-four hours following the operation. After a positive reaction was obtained the animal was killed and the pancreas removed for microscopic study.

CASE VI.—The urine before operation was negative; the urine the first day after operation was negative; the urine the second day after operation gave a positive reaction; the urine the third day after operation gave a positive reaction; the urine the fourth day after

[12] Trans. Assoc. Amer. Phys., 1908.

operation gave a positive reaction; and the urine the fifth day after operation gave a positive reaction. The dog was killed seven days after operation. An area of induration was found in the head of the pancreas, opposite the point of ligation. This lesion was the size of a large walnut, was distinctly hard, and cut with greater resistance than the remaining portions of the gland. Microscopic study of the indurated tissue showed a subacute inflammatory process, which had caused small areas of necrosis in the acini. A leukocytic infiltration, consisting for the most part of round cells, was seen in the stroma, and, to a less extent, about the acini. Proliferated connective tissue cells were also noted.

Case VII.—The urine before operation was negative; the urine the first day after operation gave a positive reaction; and the urine the second day after operation gave a positive reaction. The dog was killed on the second day. The pancreas was indurated in an area about the size and shape of a hickory nut, the lesion being directly above the ligature which still surrounded the duct. Microscopic examination showed changes similar to Case VI, but not so extensive.

Case VIII.—The urine before operation was negative; the urine fourteen hours after operation was negative; the urine the second day after operation was negative; the urine the third day after operation was negative; the urine the fourth day after operation was negative; the urine the fifth day after operation gave a positive reaction; and the urine the sixth day after operation gave a positive reaction. On the sixth day after operation an attempt was made to open the pancreatic duct at the point of ligation. This was unsuccessful on account of the induration about the duct. The first day following this procedure the urine was lost; on the second and third days the reaction was negative; on the third day typical crystals were found; and on the following day the animal died. The urine collected on this day up to the time of death gave a negative reaction. We are not prepared at this time to explain this phenomenon.

From the anatomical lesions produced by these experiments we inferred that a mechanical obstruction of the duct seems to be productive of a positive Cammidge reaction. This led us in Case VIII to attempt the removal of the obstruction caused by the ligature. Our purpose was to see if the reaction would disappear after the pancreatic duct again became patulous. As the reaction did not appear until the fifth day, and as by this time the induration was very marked, the attempt to pass a probe through the duct from its intestinal orifice was unsuccessful.

While not regarding the results of our experiments as conclusive, we believe them, nevertheless, to be very suggestive. Further research has been undertaken to determine the factors concerned in the production of the pancreatic reaction. The results of these studies will be published in our final report.

SOME OBSERVATIONS ON THE SURGERY OF THE GALL-BLADDER AND BILE DUCTS.

By W. D. Hamilton, M.D.,
of Columbus, Ohio.

The influence of microbic invasion with stagnation of bile in producing biliary infection seems to be generally admitted. The stagnation of bile is due, of course, to obstruction to its passage through some part of the biliary tract. Such an impediment may be extrinsic, or it may be located in the gall-bladder, cystic, hepatic, or common duct, or even at the end of the latter, the ampulla of Vater. The infection may be catarrhal, suppurative, or gangrenous. The frequency of gangrene of the appendix is well known; that it may involve but a limited portion of its mucosa is evident; that all of its coats may be thus destroyed at some point, or that the entire organ may become sphacelated, is a fact which has been borne out by surgical experience. That the gall-bladder is more frequently than is generally supposed the seat of gangrene, somewhere in its mucosa, at least, is my belief. Ochsner believes that the shrivelled gall-bladder so often seen accompanying obstruction of the common duct by stone is due to the cicatrization of the gall-bladder following gangrenous cholecystitis.

This probably accounts, in large measure, for the fact that operations during acute biliary outbreaks are more perilous than after subsidence has occurred. The question as to when operation should be done in acute cases, however, is a surgical and not a medical problem. The surgeon should early, if feasible, be afforded the opportunity to decide such questions. Gallstones may or may not follow these infective processes. There may be a cholecystitis, of which gallstones may be the outcome. If this be true, a patient whose illness is the result of the possession of such a gall-bladder may, at an early stage, before concretions have formed, be cured by surgical drainage, although it does not seem to have been proved that cholelithiasis always follows infections of the biliary apparatus. The importance of first eliminating the stomach, duodenum, right kidney and its ureter, and the appendix as the pathological factor is evident.

In the following case, chronic non-calculous cholecystitis was present:

Case I.—Miss K., aged twenty-eight years, in charge of Dr. Knauss, of Newark, Ohio, had typhoid six years ago, and biliary colic one year later. In the past four years pain was persistent, with occasional vomiting after food, and with tenderness rather high in the right side of the epigastrium. A diagnosis was made of chronic cholecystitis, probably non-calculous. Operation showed a small, thick-walled gall-bladder, high in the costal angle. Chole-

cystotomy was done. There were no stones; thick mucus and some bile were discharged from the gall-bladder. She has no longer either pain after food or other annoying symptoms, and is in good health.

Observation has suggested to me the possible effect of tight lacing upon the gall-bladder and bile ducts. It may drive the liver, with the gall-bladder, upward toward the costal angle, or, if to a lower level, the fundus may be found at times below the umbilicus. If in either position the liver and gall-bladder be constricted, the flow of bile through its customary channels might readily be interfered with; and as the gall-bladder is the storehouse for a considerable quantity of bile at certain stages of digestion, it is fair to assume that it may be a physiological sufferer from such constricting influences. Post-mortem evidences of the harmlessness of gallstones may be built upon error. Full and reliable knowledge of the cases is derived rather from operative experience, at which, as Moynihan aptly says, "the pathology of the living may be learned." The operation may clear the doubts and establish the pertinent pathological facts. In this and in no other way with so much certainty and beneficence may diagnosis, surgical treatment, and cure in a large proportion of cases go hand in hand. There is no known solvent for gallstones (Robson). The medical treatment may mean a resort to Carlsbad or some noted spa, while perhaps delay or palliation may imply uncertainty, or even danger of an acute attack. If the patient's general condition permit, gallstones should be removed by operation. Most of those individuals who come into the surgeon's care are obliged, if possible, for pecuniary reasons to get well, hence operative interference seems imperative in most gallstone cases.

Three of the gallstone cases in this series had inoperable cancer of the gall-bladder and liver, showing a conspicuous danger of prolonged irritation excited by gallstones.

Pancreatitis, in my experience, is a rather common complication of gallstones. Robson quotes Helly's results of 100 dissections of the common duct, showing that in 62 of them the lower end of the common duct is embraced by the head of the pancreas. Chronic inflammation affecting the head at least of the pancreas would be very liable to choke the common duct there, and produce jaundice. Robson has proved that the common catarrhal jaundice so familiar to medical men is often, in fact, due to chronic pancreatitis. A chemical pancreatic reaction of the urine has been shown by him to be present in cases of catarrhal jaundice, showing it to be a chronic pancreatitis, which operation has both proved and cured—by either cholecystotomy with prolonged drainage, or by cholecystenterostomy, thus short-circuiting the flow of bile from the liver through the gall-bladder into the duodenum.

Indigestion and pain after taking food are conspicuous symptoms of gallstones, as will be shown by the following history:

CASE II.—Mrs. M. C., aged forty-seven years, a patient of Dr. Turner of Columbus, Ohio, had been subject for ten years to agonizing pain in the stomach and epigastrium. Indigestion had been a great source of annoyance to her. Cholecystotomy performed August 31, 1907, showed one large stone in the gall-bladder and much bile sand. She is now well.

Sometimes emaciation is an added effect, as the following case with blocking by stone in the cystic duct will show:

CASE III.—Mrs. E. C., aged forty years, brought by Dr. R. Richison, of Van Wert, Ohio, had lost sixty pounds in weight in the past year. Since August, 1907, has been losing strength, and tires on slight exertion. Had been subject to stomach trouble for nineteen years, more severe of late. There were cramp-like pains across to the right side in the hepatic region. Pain usually comes on two hours after food, with cold sweats. There is a feeling of fulness and weight in the epigastrium. Last attack in November, 1907, confined her to bed three weeks. Operation, February 5, 1908, showed empyema of the gall-bladder, the walls greatly thickened, and one stone of considerable size fixed in the cystic duct. The gall-badder was removed. She is now in excellent health.

That stones may be lodged in the common duct has been emphasized by my experience. In about one-fifth of the 59 cases the subject of this report, stones were found in the common duct, and required removal, either by choledochotomy, or by coaxing them to the cystic duct, which is sometimes large enough to make them extricable through a gall-bladder incision. The importance of clearing the ducts is evident, for a patient in any of whose ducts stones remain will have further trouble. From the relative scarcity of reports of choledochotomies for the removal of stones from the common duct, I am led to believe that incomplete biliary operations are not uncommon.

The next case cited shows the chronicity of common bile duct obstruction. It illustrates also the ague-like chills, fever, and sweats from obstructive and infective cholangitis, when present:

CASE IV.—Mrs. J. F., aged sixty-five years, a patient of Dr. K. A. Norris, of Columbus, Ohio, had been subject to biliary colic for twenty-five years, more frequently of late, and accompanied by jaundice, vomiting, and fever. Operation, March 11, 1907. The small, shrivelled gall-bladder was adherent to omentum and duodenum. Cholecystotomy found one stone, large as a filbert, in the gall-bladder. A second stone, two-thirds as large as the other, lay at the duodenal orifice of the common duct. It was delivered through an ordinary choledochotomy incision. A rubber drain was stitched in the common duct, while a gauze drain was put in the gall-bladder. She recovered, had melancholia during the past year, but is quite free from former attacks, and improved in general health.

That jaundice is absent in some cases, and that even youth is

not exempt from stone in the common duct, is shown by the following history:

CASE V.—Mrs. ——, aged twenty-two years, a patient of Dr. Rank, of Newark, Ohio, had indigestion for thirteen years. There was no vomiting or jaundice. She had right infrascapular pain, and slight tenderness over the gall-bladder and common duct. The examination of the gastric contents, which is customary in all such cases in our service, showed a decided excess of hydrochloric acid, which with pain after food strongly suggested chronic gastric or duodenal ulcer, for which she had been treated for a considerable period before admission. Operation, October 2, 1907. Twenty small stones were removed. Most of them came from the gall-bladder; one from the cystic duct, and several from the common duct. The stomach and duodenum were apparently normal. Drainage was employed in the gall-bladder, right kidney pouch, and common duct. When last heard from she was gaining in weight and was in good health.

Even the hepatic ducts may be the seat of concretions:

CASE VI.—Mrs. W. B., aged forty-nine years, a patient of Dr. Case, of Mt. Gilead, Ohio, has had biliary colic at times for seventeen years, and had had jaundice with attacks. She was tender over the gall-bladder. Cholecystotomy and choledochotomy were done. The gall-bladder contained some concretions; the hepatic and common ducts were found packed with stones. She had cirrhotic changes in the liver from prolonged irritation of stones in the bile ducts. When last heard from she was in perfect health.

A concretion may be lodged so firmly in the ampulla as to necessitate transduodenal choledochotomy, as is shown by the following case:

CASE VII.—Mrs. E. W., aged forty-one years, in charge of Dr. Gahm, of Jackson, Ohio, for seven years had been subject to abdominal pain. There were four periods of invalidism. The first one lasted three months; the second two weeks; the third lasted one week in August, 1905. The last one, which extended over a period of six weeks, led up to her admission to the Mt. Carmel Hospital, February 11, 1906. Jaundice, chills, pain, and moderate emaciation had supervened. Operation, February 15, 1906. The gall-bladder was small and adherent to the duodenum. In handling, it broke open at the beginning of the cystic duct and bile escaped freely. There were no stones in it. The common duct was opened, and after a prolonged exploration a stone was found in the diverticulum of Vater. It could not be withdrawn. The common duct barely admitted the exploring finger. Firm adhesion of the duodenum to the common duct made the digital exploration more difficult, while extraction of the stone through the ordinary choledochotomy incision failed. Upon incising the duodenum, a stone the size of an olive was exposed and withdrawn from the ampulla

by lacerating the tissues overlying it. The duodenal incision was carefully stitched and the omentum secured by one suture over it. The gall-bladder was removed and a clamp left on the cystic duct and artery. A rubber drain was stitched to, but not inserted into, the common duct. A stab wound was made in the right loin through which a rubber drain was inserted. Packing was carefully used throughout the procedure. Some hemorrhoids were operated upon, as they had been causing hemorrhage and annoyance. Her convalescence was delayed by an infection of the parotid region, which required an incision for the evacuation of pus about ten days after the operation. A recent report from Dr. Gahm states that she is now in perfect health.

The following history seemed, from the result obtained, to justify another kind of procedure—cholecystenterostomy:

CASE VIII.—Miss G., aged forty-five years, a patient of Dr. Donley, of Columbus, Ohio, was admitted November, 1903. Her health had been good until six months previously, when she was seized with severe pain in the right upper quadrant of the abdomen. There were vomiting and great exhaustion. This lasted one day and was followed by jaundice. Later, after a period of subsidence, she was again seized with pain followed by jaundice, which continued, and was very marked at time of operation. There was no tenderness over the gall-bladder. The exploration, November 6, 1903, showed the gall-bladder and ducts to be free from stones. The liver was the seat of a diffuse and inoperable growth. The gall-bladder was anastomosed to the transverse colon by means of a Robson decalcified bone bobbin. She had an uneventful convalescence, and is now in excellent health, being apparently quite free from her former annoying symptoms. The growth was thought to be an extensive angioma, although no section was obtained for pathological examination.

The summary of cases given below represents all of the biliary operations performed in the practice of Dr. Charles S. Hamilton and myself between January 1, 1907, and April 1, 1908. Most of them were done in the Mt. Carmel Hospital. There were 59 patients, of whom 56 recovered from the operation and 3 died:

	Cases.	Recovered.	Died.
Cholecystotomies	29	28	1
Cholecystectomies	6	6	0
Choledochotomies	19	18	1
Exploratory, for cancer of the liver, gall-bladder, or bile ducts	3	3	0
Unclassified or miscellaneous	2	1	1
Total	59	56	3

One of the cholecystotomies was done upon a pregnant woman. She went on to term, and was delivered some months later of a well-

nourished child. Her old gastric disturbances and pain are quite relieved.

The following points may be emphasized: When the disease is confined to the gall-bladder, danger from operation is minimized. When the common duct has become the seat of obstructive and infective cholangitis, the operative risk is often greatly enhanced, for one may have a patient who is suffering both from chronic sepsis, and from cholemic intoxication as well. The infective character of the bile should be borne in mind in operations upon many of these sufferers from affections of the biliary channels. Failure to bear this in mind may lead to soiling of the peritoneum and a fatal peritonitis. Rigidity of the right rectus muscle near its upper attachment may have some significance. Either indigestion or something in the way of stomach distress are often manifest in the history of gall-bladder cholelithiasis. One may find tenderness one inch to the right and one inch above the navel in many of the common duct cases (Robson). Tenderness over the gall-bladder is quite likely to be demonstrable, if there has been a recent exacerbation of a cholecystitis. Cramps or pains through the gall-bladder to the right infrascapular region are often observed in gall-bladder or cystic duct cases.

Increasing experience suggests to us the importance of preserving the gall-bladder when salvable. The question as to the possible ultimate restoration of its function, and that of the cystic duct as well, should be carefully weighed before doing cholecystectomy.

REVIEWS.

MODERN MEDICINE. ITS THEORY AND PRACTICE. In original Contributions by American and Foreign Authors. Edited by WILLIAM OSLER, M.D., Regius Professor of Medicine in Oxford University, England. Assisted by THOMAS MCCREA, M.D., Associate Professor of Medicine and Clinical Therapeutics in the Johns Hopkins University, Baltimore. Volume IV; pp. 865. Philadelphia and New York: Lea & Febiger, 1908.

VOLUME IV of Osler's *Modern Medicine* is devoted to a discussion of diseases of the circulatory system, the blood, the spleen, the thymus, and the lymph glands. C. F. Hoover contributes two chapters: the one, an introductory chapter on different aspects of the physiology of the heart, including an interesting exposition of the myogenic and the neurogenic theories of the heart's action, and of so-called cardiac dyspnœa; and a second chapter on functional diseases of the heart, in which he describes in detail and satisfactorily, without dogmatic theorizing, tachycardia, bradycardia, arrhythmia, angina pectoris, pseudo-angina, Stokes-Adams syndrome, digestive disturbances of the heart, the relation of the sexual organs to disorders of the heart, the irritable and weakened heart, etc. He gives an interesting account of the supposed ischemia of the myocardium to which attacks of angina pectoris are attributed, believing the phenomena analogous to intermittent claudication, and to the epigastric distress after excessive eating in those the subject of gastric arteriosclerosis; and he points out the different classes of cases in which nitroglycerin, on the one hand, and morphine, on the other hand, are indicated. Diseases of the pericardium are well treated by Alexander McPhedran, considerable attention being directed to the physical signs. Diseases of the myocardium are discussed by Robert H. Babcock, acute and chronic myocarditis comprising the major portion of the discussion. The gradual development of the symptoms of chronic myocarditis is especially well portrayed, and some very valuable advice as regards treatment is given. Hypertrophy, insufficiency, and dilatation of the heart are described by Alexander G. Gibson. Among other interesting matters he gives an excellent summary of existing knowledge of the effects of long-continued and ill-advised exercise, and of hypertrophy as a compensatory process. Of the chapter on congenital

heart disease (100 pages), by Maude E. Abbott, it suffices to say that it comprises all that is really known on the subject, excellently digested and well arranged. Dr. Osler himself contributes the chapters on acute endocarditis, diseases of the arteries, and aneurysm, and, in association with Alexander G. Gibson, the chapter on valvular disease of the heart. Together these comprise 160 pages; they may be said to constitute at once the most important and the most instructive part of the book. The infectious nature of all cases of acute endocarditis is pointed out, and emphasis is laid on the fact that there is no benign or simple form. The valvular defects are described in a lucid, instructive, and entertaining manner, and considerable attention is directed to the prophylaxis and treatment. There is a short account of the rarely recognized and scarcely recognizable (except by the French) acute aortitis; and a full, orderly, and comprehensive account of arteriosclerosis, in which the influence of the four great causative factors is well elucidated—the normal wear and tear of life, the acute infections, the intoxications, and those combinations of circumstances which keep the blood tension high. The article on aneurysm is such as one might expect from an author who has already written much on the subject.

George Blumer discusses thrombosis, embolism, and phlebitis. The article is of much value, since it comprises not only a lucid statement of facts long known, but also the results of recent studies, especially the influence in causing thrombosis of agglutination of erythrocytes, of the activities of bacteria, and of the significance of calcium salts. Aldred Scott Warthin describes diseases of the lymphatic vessels and glands, and the thymus. The two chapters comprise a scholarly presentation by one whose painstaking studies and previous publications render him especially well qualified to speak with authority on the subject. The chapters on diseases of the blood are by Richard C. Cabot, and of them it suffices to say that they are worthy of their author. Purpura and hemophilia are discussed by Joseph H. Pratt—critically, comprehensively, and satisfactorily. Diseases of the spleen are well described by Irving P. Lyon.

Of the volume as a whole one may say that it is devoted to a series of diseases which are naturally related, that the classification and arrangement of subjects are very practical, and that the authors, selected with rare skill and because of proved ability, have discharged their obligations with judgment and discernment. Only lack of space precludes more detailed mention of the many meritorious articles included within the volume, which is embellished by a number of illustrations, of which several are many colored plates.

A. K.

A System of Medicine. By Many Writers. Edited by Thomas Clifford Allbutt, M.D., F.R.S., Regius Professor of Physic in the University of Cambridge; and Humphry Davy Rolleston, M.D., F.R.C.P., Physician to St. George's Hospital, London. Vol. III; pp. 1040. London: MacMillan & Co., 1907.

Volume III of Allbutt and Rolleston's *System of Medicine* is presented to us as a "rewritten rather than a revised successor of Volume III of the original edition." It contains a discussion of general diseases of obscure origin, diseases of the alimentary tract, and diseases of the peritoneum. The diseases of obscure origin include a number that often are referred to as disorders of metabolism, diseases of the joints, etc.; that they are obscure in origin is obvious from a perusal of the different articles—of which, however, one may say that they contain all that is really known of the subjects of which they treat, and some little speculation in addition. A. E. Garrod now distinguishes definnitely between what he designates rheumatoid arthritis and osteo-arthritis, which conform closely to the atrophic and the hypertrophic arthritides of Goldthwait; and to the description of these is added a chapter on the articular lesions of infective diseases (gonorrhœa, dysentery, syphilis, pneumococcic infection, etc.). The obscurity enveloping diseases of the joints is perhaps best apprehended by those that know most about them, and if Dr. Garrod has not been able to solve all of the related problems, he has given us a series of as illuminating articles on the subject as can be found in any text-book. J. Rose Bradford's revision of Lauder Brunton's article on gout should commend itself to a wide circle of readers, especially as we are now recognizing the frequency of gout, particularly irregular gout, in this country, and as the practical aspects of the subject and the treatment are well set forth. Professor Saundby's discussion of diabetes mellitus is an altogether adequate presentation of the subject, in which reference is made to the significance of reduction in the sugar-consuming capacity of the tissues in producing the morbid phenomena. More detailed discussion of the relation of disease of the pancreas would have been welcome to those especially interested in the pathogenesis of the disease.

There are many articles on diseases of the digestive tract, contributed by such well-known authors as Bradford, Ralfe, Fenwick, Spencer, Rolleston, Brunton, Allbutt, Leith, Dreschfeld, White, Still, Lockwood, Smith, Slater, Barnard, Allingham, Mummery, and Keith. Perhaps, from the very nature of the subjects discussed, it were idle to expect much that is novel; but mention may be made of two articles by Lauder Brunton—the one on dyspepsia, that presents this ubiquitous disorder in a very interesting and instructive light; and the other on constipation, which is of especial value from a practical point of view. Dreschfeld's article on ulcer of the stomach and duodenum also may be referred to as a model of its

kind; treatment by rest especially is advocated, but some brief advice relative to the indications for operative intervention also is given. The several articles on diseases of the peritoneum by Allchin and Andrews, and that on subphrenic and other forms of peritoneal abscess by Acland, are of a high order of merit. As a whole the volume well sustains the reputation achieved by those that have preceded it; that it will be long referred to as an authority there can be no doubt. A. K.

GENERAL PATHOLOGY. By ERNST ZIEGLER, M.D., Professor of Pathological Anatomy and of General Pathology in the University of Freiburg, in Breisgau, Germany. Translated from the Eleventh German Edition. Edited by ALDRED SCOTT WARTHIN, Ph.D., M.D., Professor of Pathology in the University of Michigan, Ann Arbor. Pp. 781; 604 illustrations. New York: William Wood & Co., 1908.

A NEW English edition of Ziegler's *General Pathology* is a most welcome addition to medical literature; one greets it as he would an old friend—with interest and pleasurable anticipation. Eleven editions in the original German and translations into English, French, and Italian bespeak a notable achievement, and to this one must add a great influence, direct and indirect, that the book has had upon most of the active practitioners of medicine of today; indeed, most of us have been more or less brought up on the book. The American editor only voices a general sentiment when he states that to it "alone the students of medicine during the past twenty-five years owe a large part of their medical culture, and in this respect its influence upon the recent development of medicine can hardly be estimated." In the original, Ziegler remains a final authority; the rendition into English has been made without change or omission. But since there has been some material progress in pathology since the death of the lamented author, the editor has brought the book fully abreast of the times by incorporating the important and interesting results of recent investigations, especially such as relate to the effects of Röntgen irradiation, heredity, phagocytosis, opsonins, blood plates, thrombosis, necrosis, cloudy swelling, fatty degeneration, calcification, regeneration, inflammation, malignant neoplasms, tuberculosis, syphilis, relapsing fever, spirochetæ, protozoa, etc. Of the additions, one can unreservedly say that they are worthy of incorporation in the book, that they materially enhance its value. The editor has rendered a real service by making the wealth of information contained within the book available to the English-speaking profession; let us hope that he will translate also the volume on special pathology.

A. K.

PULMONARY TUBERCULOSIS AND ITS COMPLICATIONS, WITH ESPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT. By SHERMAN G. BONNEY, A.M., M.D., Professor of Medicine in the Denver and Gross College of Medicine, Medical Department of the University of Denver. Pp. 778; 189 illustrations. Philadelphia: W. B. Saunders Co., 1908.

IN essaying to treat of the subject indicated by the foregoing title, the author has undertaken a labor of no small magnitude, a task which the reviewer believes has been meritoriously completed. On the whole, it may be said that the views set forth by the author are eminently orthodox. We believe that the value of the work would have been much enhanced if foot-note references had been appended, especially in the case of the more important publications referred to in the text, although it must be borne in mind that the book is essentially based on personal experience, with no attempt at encyclopedic scope.

It would, of course, be impossible to adjudicate all the evidence regarding the most frequent source and pathway of infection, but a very creditable *resume* of the facts has been presented, in which the main arguments of the advocates of the alimentary and the respiratory doctrines are set forth. The author concludes that, broadly speaking, alimentary infection is probably more common and respiratory infection more rare than is generally supposed. Regarding the author's views on the importance of house infection we are left in doubt, as more or less contradictory statements are made in different parts of the book.

In the chapter on physical signs, we are glad to note that undue value is not attached to the importance of inspection, as has been rather the fashion of late. He also, and very properly, advises against the employment of instrumental percussion, another fad which has periods of rejuvenation. Later on, however, he voices what we venture to believe is a somewhat unusual opinion in stating that "tympanitic resonance is found but infrequently over pulmonary cavities." Of course, it all hinges upon what is meant by tympanitic resonance, a point regarding which there seems to be a deplorable lack of unanimity among the profession. The author, however, devotes considerable space to the discussion of acoustics, and gives several pages to the consideration of different forms of stethoscopes, all of which embody much useful information. Among the numerous illustrations we find some very good examples delineating thoracic deformities, and also pulmonary skiagrams. The reviewer failed to find any reference to Grocco's sign of pleural effusion, or of Eustace Smith's sign of enlarged bronchial glands.

Considerable attention is given to the question of climate as a therapeutic measure, the author, not unnaturally, taking a view opposite to that held by many eastern physicians, who are apt

to consider this factor as relatively inconsequential. We are pleased to note, however, the absence of any unreasonable bias on this subject, which is dispassionately discussed. A very satisfactory *resume* of the development and progress of immunity and serum therapy is included, the book being brought to a close with an account of the author's personal experience—one and one-half years—with bacterial vaccines.

As has already been said, the book is one which is in large measure based upon personal experience, a fact which adds largely to its value, since it is the personal element that leaves its impress upon the mind of the reader. The keynote to the character of the book is voiced thus in the author's own words: "No teacher can assume the responsibility of describing what is not to him the actual result of his observation." G. W. N.

ADENOMYOMA OF THE UTERUS. By THOMAS STEPHEN CULLEN, M.D., Associate Professor of Gynecology in the Johns Hopkins University, Baltimore. Pp. 270. Philadelphia and London: W. B. Saunders Co., 1908.

ANY work produced by Cullen needs no introduction to medical readers. His name has always stood for careful investigation, and in the present volume, no less than in his master work upon uterine cancer, this reputation is upheld. The question discussed in this book is in the main the method of formation of the gland-islands in adenomyomas of the uterus, and the author has so presented his material that the reader is led to accept his conclusions as inevitable. In other words, the man who reads this volume with care will, at its conclusion, have somewhat the feeling that he has himself been engaged in the actual study in the laboratory and that Cullen's conclusions are his own. In order to produce this effect the material upon which the work is based has been presented in full, the photographs of the gross specimens, microscopic sections, and case histories being given.

The generally accepted idea among the majority of gynecological pathologists has been that of von Recklinghausen, who believed the glandular elements to be derived from the Wolffian duct, and although some authors have always ascribed the glandular elements in the majority of cases to the duct of Müller, there has been no definite proof of their position until the present work was accomplished. Space forbids more than a brief mention of the conclusions of the author, but in order to present his argument intelligibly it may be stated that in his series of fifty uncomplicated cases of diffuse adenomyoma of the uterus, he was able to trace the gland-islands in each case to their origin in the uterine mucous membrane, while in the

fifteen cases of subperitoneal or submucous tumors, in which it could not be expected that there would be a direct relationship demonstrable, there was found one case in which the mucosa had literally flowed into the myoma. Even if no such direct proof were available, however, the case would not be weakened, for, as the author says, it is not necessary that the uterine glands be traced by continuity to establish their origin in the mucous membrane, since the islands of glands lying deep down in the muscle correspond identically with those seen in cases in which continuity is traceable, and, moreover, they are identical with true uterine glands, are surrounded by typical stroma, and their function is retained in that in almost all cases in which cyst spaces are present the cavities were seen to contain blood in varying amounts, while in small undilated glands the presence of blood or blood pigment was frequently demonstrable.

The author's work covers a period of fourteen years, he having begun his investigations in 1894, two years before the publication of von Recklinghausen's work, and having continued them up to the present time upon material obtained from Kelly's clinic and his own service at the Church Home and Infirmary. A glance at the case histories at the end of the volume will indicate the wealth of his material. The work was undertaken as the result of one of those fortunate chances which have a peculiar faculty of presenting themselves to the trained observer, even though he be engaged in merely routine work, and this seems to us a valuable though unintentioned lesson which may be gained from the volume.

For clinical purposes the material has been divided into (*a*) growths associated with a relatively normal uterine contour; (*b*) subperitoneal or intraligamentary; and (*c*) submucous forms. The consideration of the first of these divisions comprises three chapters, a single chapter being sufficient for each of the other two. Exceedingly interesting sections are devoted to the consideration of the clinical picture presented by these tumors, their differential diagnosis, treatment, and prognosis. The two chapters upon the origin and causes of adenomyoma are among the most interesting in the whole book. The remainder of the volume is concerned with the rarer conditions met with, as the occurrence of adenomyoma with carcinoma, adenomyoma of the round ligament, etc. The book has been prepared with the utmost care from the standpoint of the publisher, while the illustrations, by Becker and Horn, are, of course, beyond criticism. The arrangement of the letter press deserves special mention in that it has been carried out in such a way that the reader who does not care to follow the author closely through his whole presentation of the subject may, by reading simply the portions in large type, get to the gist of the matter in a very short time.

W. R. N.

DISEASES OF THE EYE. By M. STEPHEN MAYOU, F.R.C.S., late Hunterian Professor, Assistant Surgeon, and Pathologist to the Central London Ophthalmic Hospital. Pp. 388; 119 illustrations, and 8 colored plates. London: Henry Frowde, Oxford University Press, Hodder & Stoughton, 1908.

BY far the best part of this book is the mechanical: the paper, type, and binding are models. As for the subject matter, this is about on a par with the usual manual, neither much better nor worse. The pathology, as might have been expected, is the best part. Much of the chapter upon refraction might almost as well have been omitted, for all the information it is likely to impart to those for whom the writer states the book is intended—students who are beginning this subject, and practitioners. The reader already acquainted with the subject can supply the omissions, but the descriptions are entirely too brief for the beginner. The chapters upon the affections of the other ocular structures are upon the whole satisfactory; the question here is simply what to omit, and this will vary with the judgment and bias of individual writers. This writer is very brief upon treatment. A few of the newer methods are given a place, such as Kronlein's operation, decompression in optic neuritis, etc. We fail to find any reference to subconjunctival injections. A couple of paragraphs are devoted to the ophthalmo-tuberculin reaction, which is credited to Calmette. The vision required for the public services in England is briefly described. T. B. S.

THE TREATMENT OF GONORRHŒA IN THE MALE. By CHARLES LEEDHAM-GREEN, M.B., F.R.C.S., Surgeon to the Queen's Hospital, Birminghan, England. Second Edition; pp. 160; 47 illustrations. New York: William Wood & Co., 1908.

THERE are several points on which stress is laid by the author which deserve passing mention. He disputes the classical interpretation of the role of the prostatic urethra in the presence of an overdistended bladder, claiming that the urethra does not widen out so as to become continuous with the vesical neck; and he presents in support of his views, which have been published previously, a skiagram of the bladder of a living subject which has been distended with a bismuth solution. He insists on the frequency of prostatitis as a complication of posterior urethritis; as well as on the rarity of a true cystitis from the same cause. He prefers local remedies to those administered internally, employing protargol in the early and silver nitrate in the later stages of urethritis. Abortive treatment he regards as practically useless. The use of the

urethroscope is described, and well illustrated. He has observed much benefit from the treatment of gonorrhœal arthritis by means of passive hyperemia. On the whole, the volume, though compendious, presents an adequate account of the disease in question; and that it has been well received is evidenced by the appearance of a second edition only two years after the first. A. P. C. A.

AIDS TO OSTEOLOGY. By PHILIP TURNER, B.Sc., M.B., M.S. (Lond.), F.R.C.S., Demonstrator of Anatomy, Guy's Hospital, London. Pp. 187. New York: William Wood & Co., 1908.

IN the compass of a volume small enough to be carried in the pocket the author has condensed a remarkably complete description of osteology, including form, surface markings, muscular attachments, and the centres of ossification No one can be an anatomist who is ignorant of osteology; and, unless well grounded in anatomy, the practitioner is rarely above the average as either physician or surgeon. The value of such works as render the acquisition of osteology easier for the student is therefore readily appreciated. The contents of the present volume are of course not original; the descriptions are borrowed mostly from Cunningham, Gray, and Quain. It is on this account, perhaps, hypercritical to blame the author for putting the appearance of the centres of ossification at such late dates. Recent investigations, especially by the aid of the Röntgen-rays, have certainly proved that these centres may be detected much earlier than was formerly thought to be the case. For instance, we have yet to see a skiagram of a child of the age of twelve months in which a centre for the capitellum of the humerus is not visible. Mr. Turner states that this centre appears in the third year. In other respects the volume can be cordially commended to students. A. P. C. A.

ELECTRICAL TREATMENT. By WILFRED HARRIS, M.D., F.R.C.P., Physician to Out-patients, Physician to the Department for Nervous Diseases, and Lecturer on Neurology, St. Mary's Hospital; Physician to Out-Patients, Hospital for Epilepsy and Paralysis, Maida Vale. Pp. 383; 24 illustrations. Chicago: W. T. Keener & Co., 1908.

TOO much praise cannot be given to this book. It has the distinction of being written by a first class neurologist, and is not only a safe and sane exposition of the principles and treatment of nervous

diseases, but it also gives the principal diagnostic points and the method of treatment in each disease. The book is mainly concerned with treatment by galvanic and faradic electricity, and in this respect it is excellent and its precepts can be followed without question. The author pays very little attention to sinusoidal and high frequency currents and still less to Röntgen rays and static electricity. It is refreshing to read a work on electrical treatment which does not claim that every disease under the sun can be cured. So many books have been written recently by electrical specialists who claim that every ill to which the human being is heir can be cured by electricity, that electrical treatment of diseases has fallen into partial disrepute and has undeservedly been classed with osteopathy and other similar cults. The fault lies in the fact that the men who treat by electrical methods take too much for granted, and writers upon this subject assume an intimate knowledge of its many subdivisions, an impossible accomplishment. This book limits itself only to treatment of diseases of the nervous system. T. H. W.

TEXT-BOOK OF OTOLOGY FOR PHYSICIANS AND STUDENTS. In thirty-two Lectures. By FR. BEZOLD, M.D., Professor of Otology in the University of Munich, and FR. SIEBENMANN, M.D., Professor of Otology in the University of Basle. Translated by J. HOLLINGER, M.D., of Chicago. Chicago: E. H. Colegrove & Co., 1908.

WE consider the title of this book a distinct misnomer. It would have been better to have entitled it "Clinical Lectures on Otology," as this is entirely the form in which it is written. As might have been expected from the standing of its authors, the book contains much of great value, but as a systematic treatise it lacks entirely the characters necessary to adapt it for the use of the student or learner in otology. The greatest unevenness is shown in the treatment of the various topics, some being treated at length, and others only sketched. Thus, the sections which deal with the anatomy of the ear show a great lack of thoroughness, while those dealing with its physiology show almost excessive minuteness. The same characteristics prevail in the entire work, certain diseases of the ear being considered at great length, and others of equal importance slighted.

To aurists the book will be of value, because they can extract from it much of original worth, and because the views expressed by its authors are, in many instances, of striking interest; but as a guide to the general practitioner and student, it cannot be so highly recommended. It is to be regretted that the translator followed so literally the German idioms. As expressed in English, there is a

most atrocious lack of attention to grammar, and some of the statements as translated are most startling, as, for instance, in the instructions for syringing the ear for the removal of cerumen, the statement is made that the cannula of the syringe is "*pressed* against the rear wall of the cartilaginous meatus," and the nurse is instructed to pull back the auricle "energetically."

It is to be hoped that another English edition of these truly interesting lectures will be demanded, and that when it is brought out, the many minor errors to be detected in the present issue will be corrected. F. R. P.

WHY WORRY? By GEORGE L. WALTON, M.D., Consulting Neurologist to the Massachusetts General Hospital, Boston. Philadelphia and London: J. B. Lippincott Company, 1908.

DR. WALTON has presented in this small volume his own personal experience in the elimination of worry from his neurotic patients. Rather full consideration is given to this symptom as the expression of various neuroses. It is questionable how far this attempt at popularizing what the medical profession has been pleased to call "psychotherapy" will be of any particular benefit to those afflicted with the neuroses mentioned. The tendency to worry is as much a symptom of neurasthenia as the fever and enlarged spleen is of typhoid fever. Neurasthenia is not the result of the worry as here manifested as a symptom, and it would be quite as rational to induce the typhoid fever patient to eliminate his fever by autosuggestion as it would be to induce the real neurasthenic to eliminate the worry. That those blessed with the nervous temperament, which is so fertile a soil for the development of neurasthenia, are prone to fuss and worry over immaterial things is well known. To such the suggestions of Dr. Walton, if there be sufficient brain power behind the nervous temperament properly to appreciate and carry them out, would be of decided value. The tendency of the brainless and the neurotic to veneer their deficiency with a smattering of anything psychological has its principal effect in leading to introspection those whose minds should be concerned only with externals.

A man with a well-poised brain will derive a certain amount of enjoyment and profit from Dr. Walton's book; a woman of the same type would probably derive more profit than enjoyment from it; a member of either sex, of neurotic type, and especially those in whom the neurotic element is associated with pathological manifestations, will derive neither profit nor pleasure, but in all probability much harm. Marcus Aurelius would at least have been much edified in learning how far his philosophical dissertations were really psychotherapy in disguise. Why worry, indeed? D. J. McC.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Pulse Pressure as an Index of the Systolic Output.—P. M. DAWSON and L. J. GORHAM (*Jour. Exp. Med.*, 1908, x, 484) have experimented on dogs, obtaining simultaneous tracings showing the mean blood pressure in the femoral artery by means of a mercury manometer, the systolic output by means of a Henderson cardioplethysmograph, and the blood pressure in the carotid and femoral arteries by means of two manometers. These records are shown on the accompanying charts and plates and bring out the different relations very closely, showing that the pulse pressure (the difference between the systolic and diastolic pressure) may be a reliable index of the systolic output. This was shown in their experiments following stimulation of the central and peripheral ends of the vagus, of the saphenous nerve centrally, of the annulus of Vieussens, in asphyxia, hemorrhage, and infusion.

Congenital Heart Disease.—M. A. ABBOTT (*Jour. Med. Research*, 1908, xix, 77) gives a careful statistical review of 400 cases of congenital heart disease which brings out several important factors more or less at variance with the accepted ideas. Some of these are the great frequency of defects of the interventricular septum, especally in combination with other conditions (149 cases among 400). Next in frequency comes patent foramen ovale (134); patent ductus arteriosus (106). The duration of life is seen to be relatively long in uncomplicated defects of the interauricular septum, patent ductus arteriosus, coarctation of the aorta, and pulmonary stenosis with closed interventricular septum; in pulmonary stenosis with a defect in the septum the duration of life is much shorter. The right chambers are chiefly hypertrophied and dilated in defects of the interauricular septum, transposition of the arterial trunks, pulmonary stenosis, and atresia. Both chambers, but

chiefly the right, are enlarged in defects of the interventricular septum and patent ductus arteriosus; the left ventricle chiefly in coarctation of the aorta. Acute endocarditis is seen to be relatively common in defects of the interventricular septum at the base and in pulmonary stenosis. Cyanosis was not marked in any case and was often absent in most of the defects of the interauricular septum. A moderate degree of cyanosis was fairly common in defects of the interventricular septum. Marked cyanosis was seen chiefly in transposition of the arterial trunks, pulmonary stenosis with defect in the interventricular septum, and pulmonary and tricuspid atresia. Cyanosis was slight or absent in a patent ductus arteriosus. In six cases defect of the interauricular and in four of the interventricular septum the cyanosis was terminal. A thrill was frequent in pure defects of the interventricular septa at the base and in pulmonary stenosis with closed interventricular septum and patent foramen ovale. A thrill was relatively rare in pulmonary stenosis with defect of the interventricular septum and closed foramen ovale. In the great majority of cardiac defects the murmur present was systolic in rhythm.

Insufflation of Air in the Treatment of Pleural Effusion.—C. ACHARD (*Semaine med.*, 1908, xxviii, 445) notes that this form of treatment has been known for some time, being first advocated by Potain in 1889. The precaution of sterilizing the air Achard does not think necessary; in passing through the tube and flask, using an ordinary vacuum or bicycle pump, the air sterilizes itself sufficiently. It takes the place of the heavy fluid, thus relieving the weight on the diaphragm and heart, and at the same time keeping up a gentle compression of the lung. He has used this method often and finds that it is of great help, seeming to prevent or delay a refilling of the pleural cavity, which is so common in some cases. It also obviates all dangers from the too rapid removal of the fluid which sometimes causes pain, cough, dyspnœa, and albuminous expectoration. The insufflation should be stopped at once when the patient complains of the least discomfort. This method of treatment Achard has found to be of great service, especially in tuberculous, serofibrinous, or hemorrhagic pleurisies, and in cases of recurring hydrothorax; in those in which the fluid is purulent, surgical measures must of course be resorted to at once.

The Influence of the Reduction of Kidney Substance upon Nitrogenous Metabolism.—R. M. PEARCE (*Jour. Exp. Med.*, 1908, x, 632) notes the importance of the influence of a possible internal secretion of the kidney, if such exist, upon general nitrogenous metabolism. Up to the present time there is little experimental or other evidence to support such a theory of an internal secretion. Pearce's experiments have been along these lines, that is, in removing amounts of kidney substance sufficient presumably to disturb the hypothetical internal secretion. His conclusions are that the removal up to three-fourths of the kidney substances causes no change in the general nitrogenous metabolism, as determined by the estimation of total nitrogen, urea, and ammonia elimination in the urine. The removal of large amounts leads to the metabolic condition of starvation; this, however, is apparently the result of the gastro-intestinal disturbance associated with extensive

kidney reduction and not to a disturbance of general nitrogenous metabolism. The determination of the amount of fecal nitrogen indicates that the gastro-intestinal disturbance is not due to diminished absorption and, except in one instance, there was no evidence of its being due to an increased elimination of nitrogenous substances into the intestine. These experiments then do not support the theory that the kidney furnishes an internal secretion having an important influence on general nitrogenous metabolism. At least if such a function exists it is not disturbed by the removal of three-fourths of the kidney substance. The metabolism in excessive kidney reduction is that of inanition dependent on gastro-intestinal disturbances, presumably due to faulty chemical co-relation. In this connection further knowledge concerning the elimination into the intestines of toxic substances is desirable.

A New Reflex between the Eye and the Circulatory and Respiratory Systems.—ASCHNER (*Wien. klin. Woch.*, 1908, xxi, 1529) has described a new reflex, the discovery of which came about in the following manner: Professor Jauragg in his lectures upon stuporous cerebral affections demonstrated a method by which a patient could be partially aroused even when he failed to respond to excessive sensory excitations. His method involved pressure on the eyes as a result of which the patient began to stir and often regained consciousness to the extent that he responded to simple questions. No explanation of this phenomenon was offered. Aschner had an opportunity of testing this in von Eiselberg's clinic upon a patient who remained under the influence of the anesthetic an unusually long time after completion of an operation. Calling, shaking, dashing cold water in the face, tickling the nose, pinching, all failed to elicit any response from the patient. Pressure on the eyes was followed by flushing of the face, deep breathing, slight movements, and finally opening of the eyes. During a repetition of the experiment Aschner felt the patient's radial pulse and was astonished to feel it disappear under his fingers. A slowing of the pulse was first noted and this immediately suggested irritation of the vagus. Two possibilities existed: (1) Vagus irritation from increased intracranial pressure and (2) a nervous reflex. On animals the experiment succeeded after opening the skull so that increased intracranial pressure was eliminated as a cause. After cutting the trigeminal nerve, especially after severing it intracranially, the phenomenon was lost. Cutting of the optic, olfactory, motor oculi, trochlear, abducens, auditory, and facial nerves produced, on the other hand, no loss of the reflex. After section of the vagus in the neck the reflex is occasionally obtainable. Whether in this case excitation of the vasoconstrictor centre with increase of the intracardial pressure occurs remains to be investigated. Effects upon the respiration are more marked in rabbits than in dogs or man. Pressure on the eyes as well as electric stimulation of all three branches of the trigeminus produced changes in the breathing, inspiration becoming spasmodic with inspiratory arrest, and likewise expiration, the latter particularly during deep narcosis. The blood pressure rises during pressure upon the eyes. Pressure upon one eye has less effect than upon both. In the exposed heart the slowing of the rhythm with evident decrease in the size of the contractions is visible and if the pressure on the eyes is increased sufficiently, the heart can be arrested in diastole.

Aschner describes other interesting points brought out in his study. The reflex is more easily obtained in narcosis than in patients who are conscious.

Hypophysis Glycosuria and its Relation to the Diabetes of Acromegaly.—It is now quite generally accepted that in acromegaly there is hyperfunction of the hypophysis, which may be of etiological importance. Since many cases of acromegaly are complicated with diabetes, BORCHARDT (*Ztschr. f. klin. Med.*, 1908, lxvi, 332) considers it possible that the latter may be due to the same cause. To test this hypothesis he has injected extracts of the hypophysis subcutaneously in rabbits. The extract was obtained from the hypophysis of man and the horse. In each animal used, following the injection of a rather large dose of extract, glycosuria occurred. The amount of sugar varied from a trace to 4.2 per cent., the glycosuria being transient and seemingly independent of the size of the dose of extract. In two animals hyperglycemia was demonstrated, the blood showing 0.41 per cent. sugar in one instance. In dogs the results were inconstant. Brain extract produced no glycosuria when injected subcutaneously. In reviewing 176 cases of acromegaly in the literature Borchardt finds diabetes in 35.5 per cent. of cases. The pancreas was normal histologically in most of the cases examined. Borchardt thinks his experiments make it probable, although by no means certain, that the diabetes of acromegaly is to be explained by hypersecretion of the hypophysis cerebri.

The Thymus in Basedow's Disease.—CAPELLE (*Münch. med. Woch.*, 1908, lv, 1826) has interested himself in the question of sudden death as a result of operation in cases of Basedow's disease. Some have ascribed death to the narcosis, others to a certain flooding of the blood with the products of the thyroid gland. But the use of cocaine anesthesia has been followed by death, and, indeed, the simple tying of the arteries has resulted fatally. A study of the literature shows that enlargement of the thymus is found in fatal cases with great frequency. Capelle finds that of 60 cases (autopsy), 79 per cent. showed a hypertrophic thymus. The operative and postoperative fatal cases had in every instance an enlarged thymus. The investigation suggests: (1) That the thymus is not necessarily enlarged in Basedow's disease. (2) That its enlargement is clinically a good indicator of the severity of the case. (3) That the deaths from heart failure after operations are, in reality, thymus deaths. Cases which show a persistent enlarged thymus should not be subjected to operation.

Salt Metabolism in Experimental Nephritis.—SCHIROKAUER (*Ztschr. f. klin. Med.*, 1908, lxvi, 182) has produced nephritis in rabbits by administering uranium nitrate and potassium chromate. Severe kidney lesions were obtained, often accompanied by anasarca. Quantitative analysis of the phosphates, chlorides, and sulphates give the following results: In nephritis with generalized œdema one finds an increased water content of the organs (muscle, liver) as a manifestation of the general retention of water. With this there is also found augmentation of the total salts of the organs which is ascribed essentially to the retention of chlorides. The phosphates are not increased in the muscles, but in the

liver the quantity is variable, being above normal occasionally. The sulphates of the muscles are within the normal limits. In the blood, however, the findings are different, the total ash showing a definite, though slight, diminution. The phosphates of the blood remain normal, while the sulphates in animals poisoned with uranium are abnormally high.

Graphic Studies of the Percussion Note.—MAY and LINDEMANN (*Deut. Arch. f. klin. Med.*, 1908, xciii, 500), in their studies upon the tympanitic and non-tympanitic percussion note, have carried out numerous experiments from which they draw the following conclusions: The tympanitic note is characterized by the uniformity of its vibration form. The tympanitic note of the abdomen arises chiefly from one kind of vibration, the ground tone (Grundtöne), which is very closely related physically to the pure tone. Additional vibrations are often found, but only in the form of harmonic overtones. As yet their determination has only revealed the first overtone. The non-tympanitic note, on the contrary, shows as its characteristic feature a complicated form of vibrations with very unequal oscillations.

Observations in Experimental Anemia.—MORAWITZ and PRATT (*Münch. med. Woch.*, 1908, lv, 1817) have found in the course of their investigations some interesting phenomena in experimental anemia of rabbits. In cases of pyrodin anemia they have noted the well-known fact that the animals soon became tolerant to the poison. This they have shown to be due to increased resistance of the red blood cells as manifested toward various hemolytic agents, such as sodium chloride solutions of different strength, alkalies, saponin, chloroform, ether, and hemolytic sera. They have obtained practically the same results with washed corpuscles. Therefore the increased resistance is not a property of the serum. In rabbits made anemic by repeated venesections no increase in the resistance of the erythrocytes is found, but when laked blood is injected intraperitoneally the resistance is increased, showing that the increased resistance is not wholly the result of the pyrodin. Four to six days after discontinuing injections of pyrodin the heightened resistance is lost. From the studies of others with human blood, *i. e.*, the finding of increase in the resistance of the corpuscles in pernicious anemia as the condition of the patient grows worse, they think it possible that some prognostic conclusions might be obtained from the study of resistance in this disease. In rabbits made anemic both by pyrodin and by venesection they find a remarkable oxidation that is not found in the normal blood. They believe the phenomenon is due to the presence of incompletely oxidized products of metabolism in the blood. Experiments have shown that the property exists in the serum, not in the red blood cells.

On Sensation to Pain in the Gastric Mucosa.—SCHMIDT (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1908, xix, 278) has made some observations on man which are of considerable interest in connection with the pain associated with hyperchlorhydria. In three patients on whom gastrotomy was performed he introduced solutions of hydrochloric acid into the stomach; 20 to 40 c.c. of 0.5 per cent. and 1 per cent. hydrochloric acid were used. They were given the acid about three hours after a

light breakfast, and psychic factors were avoided by keeping the patients in ignorance of the purpose of the experiments. None of the patients complained of the slightest pain or discomfort. Two patients died with malignant disease, and autopsy revealed perfectly normal gastric mucosæ. The experiments show, Schmidt concludes, that with normal gastric mucosa no sensation of pain is elicited from the presence of high HCl values in the stomach.

The Absorption of Uric Acid by Cartilage.—Almagia showed that the addition of cartilage from the horse to solutions of uric acid led to diminution in concentration of the solutions after they were allowed to stand for some time, owing to the fact that cartilage possesses the power to absorb urates from solution, and to store it up in crystalline form. BRUGSCH and CITRON (*Ztschr. f. exp. Path. u. Therap.*, 1908, v, 401) have repeated Almagia's experiments, as they seemed of great importance in gout, since the constant presence of uric acid in the venous blood of the arm has been demonstrated, even when the patient is on a purin-free diet. They were able to confirm Almagia's results in every particular, and then performed the same experiments, using human cartilage in place of horse's cartilage. Cartilage from the ribs and knee of an adult and from the knee of a child were used, the experiments numbering five in all. The cartilage was cut into small pieces and added to solutions of sodium urate of known strengths; some toluol was then added and the whole placed in the incubator at 37° C. for fourteen to twenty days. Subsequent analyses showed that the solutions were markedly less concentrated, and the cartilage had absorbed urate in each experiment. Sections of cartilage examined microscopically, showed the typical urate crystals as in a tophus. It is, therefore, demonstrated that human cartilage possesses the same absorption power for sodium urate as cartilage from the horse. No difference in the absorptive power was found in the cartilage taken from the child and that from the adult, nor did cartilage from the rib differ from that from the knee. Consequently Brugsch and Citron conclude that human cartilage in general is capable of absorbing sodium urate. They proved also that this ability to absorb uric acid is manifested in weak urate solutions as well as in strong solutions. They were unable to find any evidence in their experiments to support the view held by some that tophi result from precipitation of urates from the blood. Kionka has recently made the statement that many acid substances, such as glycocoll, leucin, alanin, and allantoin, accelerate the precipitation of uric acid from solutions. It remains to be demonstrated to what extent these bodies are present in the blood in gout; it is, however, well known that the blood of gouty patients is by no means saturated with uric acid. Brugsch and Citron have tested Kionka's views experimentally in the following manner: Four preparations of horse's cartilage in weakly alkaline sodium urate were made. To the first alanin was added; to the second leucin; to the third tyrosin; and the fourth was kept as a control. All the preparations were put in the incubator for five days. Analyses made at the end of this time showed the usual absorption of the urate in the control; in none of the other specimens had the slightest absorption occurred. Therefore, so far as one may judge from experiments in vitro, the amino acids are negligible in tophi formation.

SURGERY.

UNDER THE CHARGE OF

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Primary Suture in Gunshot Wounds of the Lung.—KÜTTNER (*Deut. Ztschr. f. Chir.*, 1908, xclv, 1) compares the results obtained in three cases of gunshot wounds of the lungs: one operated on under negative atmospheric pressure in a Sauerbruch cabinet, and the other two treated by conservative non-operative methods. In the first case the bullet had entered in the region of the breast and the patient was soon seized with severe dyspnœa. On his arrival at the hospital the internal hemorrhage had evidently ceased, but during the night it began anew and continued until the following morning when he was operated on. Under negative atmospheric pressure the thorax was widely opened, when a stream of blood as thick as the arm escaped through an opening in the pleura. The lung immediately expanded and the general condition improved at once. After some search and widening of the opening in the chest wall, the wounds of entrance and exit in the lung were found and closed by sutures of silk. The lung filled out close to the chest wall, and the chest wound was sutured without drainage. Primary healing followed and the patient left his bed on the eleventh day. The most striking feature was the great change for the better in the condition of the patient at the end of the operation. He left the hospital cured on the tewenty-sixth day. In the two other cases the wounds were much less dangerous, yet the results of the conservative treatment were far less favorable. One developed an empyema, for which not only was a resection of a rib done, but later a thoracoplasty. The other patient had a long convalescence, as is the result in so many cases, during which both the physician and the patient were in doubt and fear as to the ultimate result. This patient was kept in the hospital seventy-eight days and then was discharged with much deformity and in a much weaker condition than the patient operated on. Küttner could find in the literature only 5 other cases of gun-shot wound of the lung treated by primary suture. He believes that we should operate under differences in the atmospheric pressure upon the most severe, even hopeless cases of gun-shot wounds of the lung, for the purpose of directly attacking the bleeding points. He would not drain for persistent hemorrhage, but after the lung has been distended under negative pressure, he would close the chest cavity air-tight, because this aids the control of hemorrhage and the favorable course of healing. When the chest cavity is once opened for a severe primary hemorrhage, the lung wounds should be sought by all methods. Lung wounds should be tamponed only when the far more secure method of ligation or suture is technically impossible.

Removal En Bloc of Epithelioma of the Penis.—Mauclaire (*Archiv gén. d. chir.*, 1908, 11, 247) says that in the treatment of cancer we should practice wide removal of the growth and should, as far as possible, avoid inoculating the wound surface during the operation. The latter object is best attained by trying to remove en masse the infected glandular area and the tumor. Mauclaire did the following operation for cancer of the penis: An antiseptic compress was wrapped about the end of the penis to protect the operative wound from infectious or neoplasmic contamination. In the first stage he dissected the skin over the right inguinal region with the underlying connective tissue and the lymph glands down to the aponeurosis and femoral vein, in a triangular area, inward to the pubic symphysis. The second stage consisted of a similar procedure on the left side. In the third stage he made a transverse incision three fingers' breadth above the root of the penis. In raising the skin and connective tissue here a small gland may be encountered. In the fourth stage all the tissues of the penis are divided from above downward, including the lateral portion of the scrotum, so that all the lymphatics passing in this region shall be removed. All the tissues removed are thus in one piece. After ligating the bleeding points the suprapubic skin and that of the scrotum are brought together and sutured to the stump of the penis. The urethra is easily divided and separated, and its lateral margins everted and sutured to the skin of the scrotum. The margins of the rest of the wound are then brought together by sutures; a catheter is left in the bladder and dressings applied to the wound. Epithelioma of the penis is often developed from warts, placques of leukoplakia or a phimosis. Its evolution is generally very slow. Lymphatic involvement is irregular as to its location and extent. There may be from the beginning cancerous involvement of the inguinal and iliac glands. Therefore, we should remove early, and in mass, the tumor and the bilateral lymphatic region. The removal should be wide in order to increase the chances of passing the infected territory and avoiding operative grafting of the cancer.

The Various Forms of Puerperal Mastitis and Their Treatment.—Feinen (*Deut. Ztschr. f. Chir.*, 1908, xclv, 357) quotes and seems to agree with Fleck in the statement that there is no longer any doubt that mastitis is almost always due to the penetration of bacteria, by the lymph paths, from abrasions or fissures of the nipple. The bacteria are chiefly staphylococci; more rarely streptococci; in a few cases gonococci, typhoid bacilli, micrococcus, tetragenus, colon bacilli, etc. The infection occurs generally in from the second to the fourth week. Broucha reported one case in which it developed twelve hours after birth. The forms of mastitis are classified into four groups: very acute inflammations, mammary abscesses, interstitial or parenchymatous mastitis and the gangrenous form. To these may be added the tubercular. The clinical features of the acute inflammatory, the abscess, and the gangrenous forms are too well known to require special attention. The correct diagnosis of the interstitial or parenchymatous is more difficult. When only a part of the gland is diseased and the inflammation is visible in the skin only through a doughy swelling, and in the deeper part a diffuse hardening with no fluctuation is felt, and when in consequence of the radiating arrangement of the ducts and lymphatics of the gland, the

inflamed area is broad at the periphery and gradually narrows at the nipple, the diagnosis of the interstitial or parenchymatous may safely be made. In such cases there is not a total melting away of the interstitial connective tissue, nor a confluent abscess formation. It presents the picture of an intracanalicular mastitis. Feinen sums up the treatment of the different forms as follows: In cases of early inflammations the antiphlogistic treatment is best. This consists in placing the affected breast mechanically and functionally at rest. The child is weaned, the milk is not withdrawn, and a purge is given. The breast is fixed to the thorax and moist dressings applied. In from two to four days the inflammation subsides. In cases of circumscribed mammary abscesses a small incision into the abscess and suction by cupping, according to the Bier method, gives the best results. In cases of interstitial mastitis, the new operation of Bardenheuer, gives the best results. This consists in raising the breast by an incision along its lower border. The whole gland is separated from the pectoral fascia. The abscesses are then incised and drained from the posterior surface, and the wound surface cleansed of all infected tissue. It heals by granulation. Only a single operation is required and this is simple and exact and gives the best cosmetic result. There is no scar on the surface of the breast, and only a linear scar at the lower border, which is obscured by the overhanging breast. The remaining gland tissue preserves its function and only the diseased tissue is removed. Finally, because of the small amount of scar tissue, it offers the least probability of cancer formation. In the gangrenous forms the simple removal of the gangrenous parts is advised. In all cases of puerperal, tuberculous mastistis, amputation is the only treatment considered.

The Gleich Operation and its Results in the Therapy of Flat-foot.—FRISCH (*Archiv f. klin. Chir.*, 1908, lxxxvii, 324) describes the Gleich operation as performed in Eiselberg's clinic as follows: An oblique incision, a finger's breadth above the external malleolus, divides the skin, subcutaneous tissue, tendo Achillis and periosteum of the calcaneus. The margins of the wound are retracted with sharp hooks and the tuberosity is chiselled through, with as smooth a surface and as little splintering as possible. The periosteum on the far side of the bone wound is divided with a sharp knife in order to obtain free mobility of the separated piece of bone. This is displaced downward about the thickness of the small finger and slightly inward. If in any case the valgus position is especially marked, this lateral displacement of the tuberosity should be somewhat more marked. How far forward the fragment may be pushed will depend upon the angle of the chiselled surface. If this is in the right direction, as the fragment is pushed downward it may also be displaced anteriorly. While it is being held in the desired position it is fixed by a nail driven from the summit of the tuberosity through the fragment into the body of the calcaneus. The operation can be done aseptically throughout, and after the proper skin sutures are introduced and dressings applied, a plaster bandage may be put on without drainage. Frisch recommends this operation for severe cases, because of its simplicity and permanent results. The support of the arch will be so changed by the alteration in the position of the tuberosity of the os calcis, that the anterior or chief end of the

arch will be relieved and the lateral deviation diminished. By the displacement forward the leverage action of the tendo Achillis will be more advantageous. By the downward displacement the short plantar muscles produce an increase in the convexity of the plantar arch. The correction of the valgus position is obtained by the displacement of the tuberosity inward. A few months are necessary before the patient can walk or stand. The wearing of a brace or splint after the operation will not be necessary as the improvement is spontaneous.

Two Cases of Gallstone Ileus; Operation; Recovery.—NEWBOLT (*Lancet*, 1908, clxxv, 797) says that the diagnosis was not made in either of his two cases before operation. The fact that the obstruction is a mechanical blocking of the bowel and that those symptoms depending upon a direct interference with the vascular supply are absent, may help us in the diagnosis. In both cases the stones were found in the small intestine not far from the ileocecal valve. They were both nearly of the same size. The first measured two inches in length, one and one-half inches in diameter, and three and one-half inches in circumference; and the second was only one-quarter of an inch smaller in each dimension. Each stone had a constriction at the end nearest the duodenum, and in one case the stone was fractured at this constriction. What impressed Newbold most was the unfamiliar type of the symptoms of obstruction in both cases. Some days after the beginning of the attack, neither of the patients looked as ill as one would have expected and the soft though distended abdomen with the absence of tenderness on pressure, was most marked. A stringent cross examination failed to elicit any history of gallstones even after operation.

Notes on 679 Operations Performed under Spinal Anesthesia (Cocaine or Stovaine) by Tuffier's Method.—SABADINI (*Lancet*, clxxv, 1213) says that the early contributions of Corning, Tuffier, and others had established the fact that the introduction of cocaine into the spinal column produced widespread anesthesia without circulatory or respiratory disturbances, and that cocaine determined no grave changes in contact with the nerve elements. Sabadini's 679 operations included a large variety of laparotomies and operations on the limbs. They were always below the level of the umbilicus, the anesthesia extending upward as a general rule to within two fingers' breadth below the breasts. Yet he removed three mammary cancers by this method and did a resection of the elbow. The dose in these 4 cases was 3 cg. for the first 3, and 4 cg. for the fourth. To insure diffusion of the cocaine the patient was kept in the Trendelenberg position for ten minutes after the infection, but anesthesia was incomplete in each case and chloroform was added. He has not repeated the experiment. The number of failures was about 11 per cent., and they were probably due to idiosyncracies or to the fact that the anesthetic dose varies with the individual. The subjective phenomena occurring between five and fifteen minutes after injection are such as pallor, sweating, nausea, vomiting, and occasionally but rarely marked apprehension. Epileptoid tremors of the lower limbs and fatal syncope may develop. The frequency of nausea and vomiting has been reduced 50 per cent. by giving the patients their breakfast before making the injection. Sabadini has had no case of

fatal syncope. He recognizes the following contra-indications to this method of anesthesia: Advanced cachexia, bilateral nephritis with scanty urinary secretion, myocarditis, pericarditis with effusion, and non-compensated cardiac affections. These absolutely prohibit the use of cocaine. The only two untoward consequences at a later period have been headache and rachialgia. All accidents that occur are to be ascribed to a defective technique and not to the method per se. The only real drawback to the method is that in certain nervous and alcoholic subjects the anesthesia is not complete. It may be employed in patients from ten to fifteen years of age up to extreme old age. Although stovaine was not given a satisfactory trial, on the whole the advantages appear to be in its favor.

A New Method of Sterilizing the Skin for Operations.—GROSSISCH (*Zent. f. Chir.*, 1908, xxxv, 1289) has had a large experience in the treatment of wounds resulting from accidents. These are frequently difficult to render aseptic, especially when they involve the hairy part of the scalp, neck, axilla, or scrotum, or the fingers and toes. In his first case Grossisch painted the surface of a broad lacerated wound and the surrounding skin with the tincture of iodine without any washing. He sutured the wound completely, coated the sutures with the iodine and applied the usual sterile dressing. Healing by first intention followed. This method has since been repeated many times with the same result, provided there was already no preceding sign of infection of the wound. When a preliminary cleansing of the wound and surrounding skin by soap and water was made, the healing was not so favorable and points of suppuration developed here and there. This method was later applied to small operations, the hair being first shaved dry, and the field of operation then covered with the tincture of iodine. Perfect healing by first intention was usually obtained. Microscopic examination of a piece of skin treated by iodine showed that the iodine had penetrated into all the clefts and spaces and lymph radicles. This capacity for penetration is due to the alcohol present. Water or watery solutions penetrate only incompletely and superficially. Grossisch has used this method in operations for free inguinal and femoral herniæ and incarcerated inguinal. All healed without any disturbance. The method has also been employed successfully in other major operations. The same scrupulous care must be observed in cleansing the hands, instruments, and dressings, as in operations by the usual methods.

Compensatory Re-arrangement of the Space in the Chest Cavity after Amputation of One Lung, together with Observations on Operative Mediastinal Emphysema.—FRIEDERICH (*Archiv f. klin. Chir.*, 1908, lxxxvii, 647) says that mediastinal emphysema may become a fatal complication after operation on the lung, especially when the operation invades the lung near the hilus and when the opened bronchus has not been closed properly. Seven days after amputation in the pneumatic cabinet of the lung of a dog, when the recovery was progressing favorably, the dog suddenly began to fail and to develop a subcutaneous emphysema over the chest. This progressed rapidly and extensively, and the dog died in six or seven hours. Postmortem examination showed beside the general subcutaneous emphysema, interstitial emphysema along

the deep muscles of the neck, enormous emphysema of the mediastinum, pericardium, and the whole retropleural, peripleural, and retroperitoneal tissue. At the right hilus there was found a loosened ligature, which had been applied to a divided bronchus, and this bronchus had retracted inward into the mediastinal space. Opening of the chest in the pneumatic cabinet, with resulting removal of the air, might have overcome the indirect effect of the mediastinal emphysema on the circulation and respiration. An almost analagous case is reported by Friederich, following removal of the left lung in a woman, but in this case the autopsy did not reveal the source of the escaping air. A septic pleurisy also developed in this case. In those animals in which the amputation of the lung had been done and the ligature had been effective in maintaining the closure of the bronchus, and the asepsis was good, the operation was quickly and effectively carried out, and no symptoms of inflammation developed. The animals lived, were active, had good appetites, and increased in weight. This shows that the remaining organs adapt themselves to the altered relations rendered necessary by the vacant space left by the removal of the lung. This is brought about by a change in position of the soft tissues and a sinking in of the ribs on the side operated on, so that the space vacated by the removed lung becomes obliterated. This is well shown by the illustrations of specimens from dogs operated on and later killed. Absolute healing may thus follow the removal of one lung. The defect becomes filled, by the displacement of the heart and mediastinum toward the affected side, by vicarious emphysema of the remaining lung, by ascent of the diaphragm, and by flattening of the ribs on the affected side.

THERAPEUTICS.

UNDER THE CHARGE OF

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Vaccine Therapy and Therapeutic Immunization.—WRIGHT (*Practitioner*, 1908, vi, 565) reviews the conclusions which have been established by his own results in vaccine therapy and auto-immunization and by those of his fellow workers. These conclusions are the following: (1) Vaccine therapy is applicable not only to localized infections, but also to general septicemic diseases. (2) Spontaneous auto-inoculations occur not only in general septicemic diseases, but also in cases with localized diseases in which the focus of infection has attained to a certain development. (3) Auto-inoculation can, in the case of localized disease, be artificially induced by massage, by active and passive movements, and by active and passive hyperemia. (4) Such artificially induced auto-inoculations can be turned to useful account in diagnosis. (5) The success of certain empirical methods of treatment,

notably the Bier method of passive congestion, is probably largely dependent upon the fact that it induces adequate and not excessive auto-inoculations. Wright further considers the possibility of achieving the desired improvement apart from the determination of the opsonic index. There is associated with this point the question as to whether the technique used for the determination of the opsonic index gives accurate and useful results. He is of the opinion that injections of bacterial vaccines should not be undertaken entirely in the dark. He believes that both vaccines and the human organism are too variable and inconstant factors to allow even an approximation to the fixing of a definite dose applicable to all conditions. In dealing with vaccines, one can never leave out of consideration the difference in different strains of the same organism. Some minute difference in the mode of preparation, or perhaps some change occurring spontaneously during preservation, might affect the strength of the vaccine products. But a greater factor exists in the different effect produced by the same dose of vaccine in the healthy individual as compared with that in the infected patients, and in the cases of severe infection as compared with the result in those of light infection. Thus, when it is difficult to predict the result of one inoculation, it is much more difficult to predict the result of a series of inoculations. In a few individual cases a proper dose may be arrived at which will give uniform results. This is true in strictly isolated local infections, such as a furuncle. When one adheres to a given dose, there is a possibility of two errors. The doses might be too small, and have little or no effect, or, on the other hand, they might excite a marked negative phase and so do much harm. In taking up the suggestion that the clinical symptoms of the patient may furnish a guide, he considers four classes of cases. There are cases of localized infections which the clinical observer can see for himself and learn of every change which occurs in the focus of infection. The most typical examples of these are furunculosis, sycosis, and suppurating acne which are usually due to staphylococci. In the same class there are the streptococcic infections of the skin and subcutaneous tissue, which take the form of impetigo, serous furuncles, erysipelas, and lymphangitis. He also includes in this class infections of any organ in which by examination of secretions or excretions one may obtain an idea of the inflammatory process.

With the subjective symptoms as a guide in such cases, and with such objective signs as we can elicit, we may judge whether the dose has been moderate, small, or excessive. An improvement for a brief period followed by an early relapse would indicate too small a dose. If the patient grew immediately worse, we would assume an excessive dose. He points out some errors, however, which may result if too great dependence is put on clinical symptoms: (*a*) The clinical symptoms may convey quite an erroneous idea of the real conditions of the local infection. This is true in mixed infections, in which incidentally the secondary infection may increase in extent and obscure the clinical picture. (*b*) The clinical symptoms of the local infection may give an entirely wrong idea of the general infection. (*c*) The anti-bacterial power of the blood of a patient in good, general condition cannot be assumed to be at all uniform.

There are cases of strictly localized infection in which the process is

more or less chronic, in which the information indicating an advance in the process as given by clinical signs and symptoms is often too late. This class comprises cases of tuberculous adenitis or arthritis, phthisis, and lupus. In acute febrile conditions the general rule, that with the subsidence of the temperature the protective substances increase, has many exceptions. Finally, there is the class of cases in which all local and general symptoms are in abeyance. This class includes cases of the other groups which are apparently cured. Wright claims that the important question relative to the establishment of immunity can be answered in all cases only by a determination of the opsonic index. He believes that the technique for the determination of the opsonic index furnishes accurate and useful information with respect to the patient's progress. He explains the inconsistent results of other observers either by faulty technique, in the necessary mechanical manipulation, or by lack of required patience.

Wright mentions a number of therapeutic measures which bring the antibacterial agencies of the circulating blood into effective operation upon the microbes at the site of infection.

Among the measures are active and passive hyperemia. He believes their beneficial effects are produced by auto-inoculation. Active hyperemia may be induced by hot fomentations, rubefacients, or heat in any form. Passive hyperemia is usually obtained by the well-known method of Bier. Wright says that diminished coagulability of the blood is associated with increased transudation of lymph, while increased coagulability leads to a diminished transudation of lymph. He believes also that calcium salts, especially the lactate, have the power to increase the coagulability of the blood, and that citric acid diminishes it. Thus, he thinks it possible to hasten the absorption of a transudate by giving calcium lactate or to secure an effusion of serum by the use of citric acid. He points out the advantage of determining a flow of lymph rich in anti-bacterial power to the infected area. For this purpose he advises the use of wet dressings of one and a half to four parts of salt and one part of citrate of sodium dissolved in 100 c.c. of boiling water. The surrounding skin should be protected by vaseline to prevent excoriation. He considers that the various surgical procedures of evacuating abscesses are all means to an end, the means of bringing the antibacterial agencies of the blood into effective operation. Therefore, he believes in early incision, before the formation of pus.

A Specific Ferment Therapy for Diabetes.—ZUELZER (*Ztschr. f. exp. Path. u. Therap.*, 1908, v, 306) showed in a previous paper that in experimental animals injection of a pancreatic extract prevents the production of adrenalin diabetes. In this communication Zuelzer gives the results obtained by the injection of the extract in experimental diabetes due to extirpation of the pancreas and in diabetes in man. The extract was prepared from pancreatic glands taken from animals at the height of digestion. The animal experiments were few in number, but the results obtained were quite constant, that is, diminution of the quantity of sugar excreted in the days following the injection. The experiments on animals were interrupted by an opportunity to try the extract in man, and had not been completed at the time of publication. The first human patient was a man, aged fifty years, in whom diabetes

had been discovered three years previously. On strict diet the sugar amounted to 6 per cent. Following amputation of the left leg for gangrene, acidosis with coma developed and the patient's condition was desperate. Accordingly, he was given a subcutaneous injection of 3 grams of pancreatic extract dissolved in 8 c.c. of water. On the following day a second injection containing 5 grams was given. The urine was lost during the days subsequent to the injections, but there occurred a marked improvement in the general condition of the patient, especially in his mental condition. Seventeen days after the first injection was given the patient died, before a fresh supply of extract could be obtained. The results demonstrated, however, the apparent harmlessness of the extract. The second patient was a man, aged twenty-seven years, admitted to Prof. Kraus' clinic six months after the diagnosis of diabetes had first been made. The amount of urine varied between 1400 and 3000 c.c., sugar between 2 per cent. and 6.4 per cent., and acetone and diacetic acid were constantly present. Following the first small injection (1 c.c. intravenously) the sugar fell to 1.3 per cent. in 1400 c.c. of urine, acetone, and diacetic acid being present. The second injection was larger, containing 2 grams of extract. Acetone and diacetic acid completely disappeared from the urine on the next day, and the urine contained neither of these substances for three days; glucose gradually diminished until only a trace was found on the third day after the second injection. Subsequently the sugar gradually increased in quantity and diacetic acid and acetone reappeared. Further observations in this case were impossible, as the patient left the hospital. In six other diabetics between six and sixty-five years of age, injections of pancreatic extract were tried, and in all the results were uniform and constant (except in a few instances in which inactive extract was demonstrated), the glucose always being diminished and usually entirely absent from the urine in two to three days after the injection, the same also holding good with acetone and diacetic acid. On several occasions the injections were followed by chill, rise in temperature, and, less often, by a stomatitis, the symptoms passing off in one to two days. In all the experiments no change was made in the diet of the patients after the injections. In the future Zuelzor proposes giving smaller doses at more frequent intervals, hoping thus to avoid the unpleasant consequences. His conclusion is that it is possible to cause sugar, diacetic acid, and acetone to disappear from the urine of diabetics by the injection of pancreatic extracts. To what extent this fact may be utilized therapeutically remains to be determined.

The Treatment of Diphtheria, Scarlet Fever, and Tonsillitis by Pyocyanase.—SAUER (*Deut. med. Woch.*, 1908, xxxvi, 1541) has used pyocyanase as a spray in 39 cases of various throat infections. These cases included 14 cases of diphtheria, 8 of the sore throat of scarlet fever, and 17 of severe tonsillitis, 3 of which were cases of Vincent's angina. Every case was diagnosticated by a bacteriological examination. Laboratory experiments showed that the preparation had a solvent action upon diphtheritic membrane. The growth of diphtheria bacilli in cultures was in part inhibited, but there was no effect in neutralizing the diphtheria toxin. An ordinary throat spray was used and the throat was sprayed with the solution three to four times a day. For a half hour

after the spraying the patient must not gargle. The throat may be sprayed through the nose when necessary. Children soon get accustomed to its use. Clinically Sauer observed a rapid diminution of the diphtheritic membrane, with a rapid disappearance of the diphtheria bacilli from the throat. The sore throat of scarlet fever was rapidly relieved and the membrane disappeared in three to four days. Vincent's angina was cured in from two to three days. Cases of ordinary tonsillitis rapidly improved, both as regards the disappearance of the membrane and the subsidence of the fever and general symptoms. He does not believe that pyocyanase can take the place of diphtheria antitoxin, although it may be a useful adjuvant in the treatment of diphtheria. It may also allow the use of smaller doses of antitoxin than are usually thought necessary.

The Treatment of Tetanus by Means of the Local Application of Lipoid Substances.—BROCKENHEIMER (*Archiv f. klin. Chir.*, 1908, lxxxvi), in his investigations of this subject, has taken advantage of the known power of some lipoid bodies to bind toxins. This fact is notable in the case of snake venoms which are bound by cholesterin and of botulismus toxin, which act similarly with other lipoid bodies. The fats used by the author were olive oil, cod-liver oil, liquid paraffin, vaseline, and a salve of Peruvian balsam. The experimental research was conducted on guinea-pigs, which are quite susceptible to tetanus, and the inoculations were made so as to approximate the conditions of infection in man. The fats were applied to the area of infection. The best results were secured with Peruvian balsam salve, which prolonged the period of incubation to twice that of control animals, and caused the tetanus when developed to appear less virulent than in the controls. Brockenheimer reviews the cases of tetanus occurring in von Bergman's clinic for the last twenty-five years. There have been in this period 29 cases of tetanus, with a mortality of 86.2 per cent. Of 20 cases treated by means of antitoxin, 3 recovered, and in these 3 the period of incubation was prolonged, allowing a more efficient antitoxin treatment. Brockenheimer considers the proper treatment of wounds suspected to be infected with tetanus: (1) Cleansing and washing out with hydrogen peroxide, since this checks the growth of tetanus bacilli. (2) Applications of Peruvian balsam salve to delay the incubation period. (3) The daily use of antitoxin during the doubtful period. Amputation is advised in the cases of local tetanus which develop in the first two weeks after injury.

The Treatment of Gout.—L. A. AMBLARD (*Arch. gén. de méd.*, 1908, lxxxviii, 411) gives in detail a review of the recent advances in the treatment of gout, especially as regards the dietetic régime necessary for the best results. After a thorough review of the literature he is inclined to believe that the uric acid is most probably kept soluble by the action of thymic acid, hence the importance of the use of this latter agent therapeutically. As high temperatures destroy the combinations of this acid with the purins, rare meats are more desirable than those well cooked. Food stuffs, poor in purins, should be given as much as possible (these may be found in Hall's dietetic tables accompanying the article). White meats contain nearly as much purins as dark meats,

as do also beans and oat meal, so that the best articles of diet are milk, butter, fresh cheese and eggs, and possibly a little red meat each day. As regards the medicinal treatment the wine of colchicum is of most importance in the acute cases, many other drugs being used during the course of the disease for their supposedly dissolving effect on the uric acid; these are the various alkaline drugs—salicylates, piperazine, aspirin, and thymic acid, which latter Amblard advocates on account of its soluble action on the uric acid. Finally the free use of mineral waters and of exercise are of the utmost importance.

PEDIATRICS.

UNDER THE CHARGE OF

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Spontaneous Hemorrhage from the Ear Terminating in Death.—H. HALASZ (*Archiv f. Ohrenheilk.*, 1908, lxxvi, 78) reports the case of a child of two weeks, born at seven months, which died after bleeding from the right ear, the hemorrhage extending over a period of eight days. Such cases are extremely rare and in most instances are preceded by a suppurating condition of the ear. There are but 2 cases (his own being one) in which no such illness preceded the hemorrhage. At first the blood came from the ear, flowing but slowly with occasional cessation of one or more hours. After a few days a sausage-shaped mass developed at the right side of the neck, which ruptured, with the result of blood escaping from this wound also. About this time the child became jaundiced. The mass mentioned was three inches long, the size of the middle finger, hard, not pulsating, and the blood escaping from it as well as from the ear was dark red. No operation was permitted and death occurred on the eighth day. In the absence of an autopsy the cause of the bleeding could not be accurately determined. The bleeding was evidently venous—jugular vein or transverse sinus—as proved by the slow flow, the dark color, and the absence of pulsation in the mass, which latter was probably the thrombosed jugular vein. The cause might have been syphilis, tuberculosis, acute yellow atrophy, or leukemia.

Congenital Dislocation of the Hip Treated according to the Method of Lorenz.—VAN DEN BERGH (*Ann. et bull. de la soc. de méd. d'Anvers*, 1908, lxx, 17) reports 15 cases of congenital dislocation of the hip, 7 of which were right-sided, 3 left-sided, and 5 bilateral. Fourteen of the patients were girls and one a boy. Three were less than two years old; 2 of these were still under treatment, while the third died of meningitis, two and one-half months after the reduction; 4 were three years old and 3 of these recovered, the last remaining without improvement; 1 of these cases was operated on ten years ago; 1 at four operated

on four years ago remains well; 3 were operated on at five, with two known good results; the third was lost sight of; 1 patient at six was not improved; 1 at eight and 1 at eleven were cured; another at eleven was made somewhat better. Van Den Bergh has not had radiograms made to control his good results, of which there were 8 in all, and thinks that in several cases the head was fixed in anterior luxation, but with perfect and permanent functional result.

Examination of Eyes in the Schools of Brussels.—P. DE RIDDER (*Ann. d'ocul.*, 1908, cxl, 27) has examined the eyes of 2820 children of the schools of Brussels. Between six and eight years there were 835 children; 353 (42 per cent.) had abnormal vision; 197 (23 per cent.) were hypermetropes; 48 (5.5 per cent.) myopes, and 83 (10 per cent.) had astigmatism. Between nine and ten years there were 869 children examined; 333 (40 per cent.) had abnormal vision; 172 (19 per cent.) had hypermetropia, 74 (8.5 per cent.) myopia, and 69 (8 per cent.) astigmatism. Between the ages of eleven and twelve, 735 children were examined with 316 (42 per cent.) of abnormalities; 156 (21 per cent.) had hypermetropia, 80 (10 per cent.) myopia, and 61 (9 per cent.) astigmatism. Of 376 children between the ages of thirteen and fourteen examined, 208 (44 per cent.) were found to have abnormal vision; 85 (22 per cent.) of these had hypermetropia, 69 (18 per cent.) myopia, and 45 (12 per cent.) astigmatism. In all there were 607 (21.5 per cent.) hypermetropes, 289 (10 per cent.) myopes, and 272 (9 per cent.) astigmatics. It can be seen from this that hypermetropia and astigmatism are not increased by the work of the schools, but in myopia the proportionate increase is quite marked, this being due directly to the school studies; the same condition is reported from other parts of the world. He concludes from this, that the eyes of all the scholars should be examined, and means to correct their vision devised; on account of the gradual development of myopia the surveillance should be continued throughout the school years to note the appearance of visual alterations; as the scholars quit school they should be advised as to the best line of work for them to take up.

Hemorrhage after Excision of the Tonsils.—Fatal hemorrhage after tonsillectomy or adenoid operations is very rare, and when occurring it may be immediate (connected probably with the operation) or secondary. The former is due usually to injury of the neighboring vessels, the latter to hemophilia, although this disturbance may be the cause of immediate hemorrhage also. HAYMAN (*Archiv f. Laryng. u. Rhin.*, 1908, xxi, 15) reports the case of a boy of fourteen, in whom all three tonsils were removed because of frequently recurring violent attacks of tonsillitis. He had always been a perfectly healthy boy, and there was no history of hemophilia in the family. In earlier years he had been operated on for adenitis without appreciable hemorrhage, and the only thing known to call attention to the disturbance lay in the fact that light injuries to his fingers always resulted in prolonged and marked bleeding. The operation was not accompanied by especial bleeding and what there was ceased completely within a short time. Two hours later blood trickled into the pharynx from the nose in a steady stream, and could not be checked by ordinary measures; later the pharyngeal

tissue began to ooze also. Hydrogen peroxide and styptic powders did not avail, but after the nose was tamponed, bleeding therefrom was checked for a time. It reappeared again, and in spite of adrenalin, gelatin, suturing of stumps, tamponing of pharynx, and other procedures it continued, terminating in death sixteen hours after the operation. The autopsy showed a perfectly normal state of the internal organs, and careful search did not reveal any injury of the vessels of the neck. Hayman considers this a case of hemophilia, as no other cause could be discovered in spite of careful consideration.

Pretracheal Abscess in a Case of Scarlet Fever.—GIUSEFFI (*Allg. Wien. med. Woch.*, 1908, liii, 373) reports the case of a girl, aged nine months, who had recovered only a short time before from an attack of measles. She was suffering with a sore throat, from the exudate of which many cocci and some few bacilli were isolated. On the third day of the disease the typical scarlet-fever eruption appeared, and with this was noted a disappearance of a slight hoarseness of the voice. The child had high fever for four days. On the tenth day of the exanthem moderate signs of a stenosis were noted, not sufficient, however, to make an operation seem necessary. The child died during the night from a sudden paroxysm of asphyxia. An elastic tumor the size of a walnut was found beneath the sternohyoid and sternothyroid muscles, which when incised was found to contain thick yellow pus. The abscess extended from the beginning of the trachea to its bifurcation without, however, exerting any pressure upon the pneumogastric or recurrent laryngeal nerves or the œsophagus. The right pulmonary apex was the seat of bronchopneumonic foci. The thymus was attached to the lower pole of the abscess wall. Streptococcus pyogenes was isolated from the pus in pure culture. This organism had probably entered the pretracheal glands during the attack of measles. Giuseffi has not been able to discover a similar case in the literature, the few he has been able to note being due to intubation trauma, or aspiration of foreign bodies.

Prophylaxis of Umbilical Tetanus at Saigon (Cochinchina).—At the suggestion of R. MONTEL (*Ann. d'hygiéne et de méd. col.*, 1908, xi, 72) a maternity was instituted at Saigon in Cochinchina, and the midwives of the district trained in aseptic obstetrics. This was followed within a few years by a reduction in the tetanus mortality from 30 of every 100 deaths to 2.52, and by a fall of the general mortality of the infants less than one month old from 37.33 out of every 100 born to 21.73 (1905), 13.92 (1906), and 10.22 (1907). Cutting the umbilical cord with sterilized scissors and tying it with an aseptic ligature sufficed to prevent the greater number of tetanus infections. A number of other precautions to diminish the general mortality from other diseases (gonorrheal ophthalmia, hereditary syphilis, etc.) has also been taken.

OBSTETRICS.

UNDER THE CHARGE OF

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Hebosteotomy Compared with Other Procedures in the Management of Labor in Contracted Pelves.—PFANNENSTIEL (*Surgery, Gynecology, and Obstetrics*, October, 1908) has found that hebosteotomy enlarges the transverse diameter of the pelvic inlet on the average 4 to 5 cm., and occasionally 7 cm. The anteroposterior diameter is increased 1 cm., or at most 1.5 cm. The pelvic outlet is enlarged only about 2 cm. in the transverse diameter, and 0.5 in the anteroposterior. A conjugata vera of 8.5 cm. must be present for the successful passage of a normal child. Accordingly, the operation is indicated only when the conjugata vera is 7 cm. or more. In a flat pelvis in which the inlet is contracted, but in which the outlet is large, the operation may be employed with a true conjugate of 6.75 cm. In generally contracted pelves one should not go below the limit of 7.5 cm., because the outlet is also contracted. Lacerations are very apt to occur in such cases from the cut ends of the bone. There is no upper limit to the operation, which may be chosen upon the comparative size of mother and child. It is then of the greatest importance to ascertain this fact in the higher grades of pelvic contraction. Cesarean section is indicated in flat pelves with a conjugata vera under 7 cm., in generally contracted pelves with a conjugata vera under 7.5 cm., and in the case of a very large child, with a conjugata vera of 8 cm. In comparing results of hebosteotomy and Cesarean section, the mother is exposed to about the same risk in both operations, an average mortality of 4.5 per cent. The infant mortality in hebosteotomy is 7 per cent.; in Cesarean section, 1 per cent. For success in both it is important that no previous effort at delivery should have been made, and that the condition of the patient should be absolutely aseptic. If infection has occurred, then both operations should be declined. Version should be avoided after the operation, but the high application of forceps is permissible when infection is absent. This attempt must be made very cautiously, and if the head is not readily delivered then craniotomy should be done. When the patient declines the operation, in flat pelves of moderate contraction, with the child of moderate size, prophylactic version is advised. Induction of labor before the thirty-sixth week, when the head is proportionate to the pelvis, gives good result. If the pelvis is generally contracted, the true conjugate must be not less than 8 cm., and if flat, 7.5 cm. Careful, aseptic technique is necessary, and in flat pelves dilatation with bags, followed by prophylactic version, may be employed. In generally contracted pelves bougies may be used and spontaneous labor encouraged as much as possible. The use of forceps will often be indicated, but the mortality for the children in induced labor varies from 2 to 18 per cent. The operation for the child is less safe than hebosteotomy or Cesarean section. The operation is to be performed by an experienced surgeon only.

Pfannenstiel's method in hebosteotomy is as follows: The incision, about 1.5 cm. long, is made on one side in the groove between the labium minus and labium majus. It is parallel to the descending ramus of the pubes, and is made down to the bone. The soft parts behind the pubic bone are separated by an elevator and the fingers. Bumm's needle is introduced from below upward to the tubercle of the pubis, with saw attached, pulled through, and the bone sawed subcutaneously. The wounds above and below are closed with silkworm-gut suture, and the patient is delivered. Spontaneous labor is not waited for to avoid pain and delay. In four cases labor was complicated by prolapse of the cord, and in three by excessive pressure upon the head. When the soft parts are very narrow, Pfannenstiel makes a prophylactic perineovaginal incision on the same side with the incision through the bone. This he thinks prevents lacerations of the soft parts by the bone.

Puerperal Salpingitis.—FRIEDMAN (*Surgery, Gynecology, and Obstetrics*, October, 1908) draws attention to puerperal salpingitis, and describes the symptoms in 21 cases. He distinguishes a gonorrhœal variety and that due to other infections. This disorder usually appears about the third day, with rise of temperature to 102° F. or 103° F. If the infection is limited to the tube, the pulse does not rise in proportion to the temperature. The patient complains of pelvic pain on the affected side, and lies flat with the leg drawn up. There is moderate tenderness on deep pressure. Spasm is usually absent. The lochia are at first normal, then contain pus. If the tube is not closed, and drains, very little pain is present. Three types of this condition may be observed: The first, in which the tube is closed at the peritoneal extremity, but drains into the uterus, pain and temperature are moderate or absent, but the lochia very soon contain pus. When both ends of the tube are occluded the lochia are normal, but pain and temperature are much increased. Occasionally the tube ruptures into the peritoneal cavity. When the uterine extremity of the tube is closed, the peritoneal end open, the temperature high, then peritonitis is apt to develop from the escape of pus into the peritoneal cavity. Both ends of the tube are rarely ever open. When the right tube is affected, then appendicitis may be suspected also. As the prognosis is good, the treatment usually required consists in the administration of codein, and absolute rest. Interference is rarely necessary, but should be undertaken if the case does not promptly improve.

Traumatic Rupture of the Uterus and Bladder during Labor at Full Term; Hysterectomy, Repair of Bladder, and Recovery.—BROWN and SWAHLEN (*Jour. Amer. Med. Assoc.*, October 24, 1908) report the case of a multipara attended in labor at first by a midwife. Later a specialist was summoned, who made an ineffectual attempt to deliver with forceps. The head was transverse above the pelvis but had not engaged. The lower uterine segment was very thin and reached to the umbilicus. When forceps failed, the patient was advised to go to the hospital, but refused. The back of the child was to the mother's right. An attempt was then made to deliver by version, and one leg of the child was brought into the vagina. At this point the uterus ruptured, and the child could be felt upon the left side of the abdomen, and the contracted uterus upon the right.

The patient was finally transferred to a hospital, and upon opening the abdomen a large quantity of blood and amniotic fluid was found. The child was readily delivered. The uterus was torn across the lower uterine segment, extending two-thirds around the cervix and into the body of the uterus. Both uterine arteries were bleeding; the bladder had been ruptured. The broad ligaments were clamped and the uterus amputated above the cervix, the rent of the bladder repaired with silk suture, and the peritoneum was stitched over the uterine stump. The abdominal cavity was flushed with hot saline solution and immediately closed. The patient made an uninterrupted recovery.

[This case recalls a recent experience of the reviewer: A physician had attempted twice with Tarnier's forceps to deliver a multipara, who had had difficult labors. The head of the child was movable above the pelvic brim. The forceps slipped. At the second application bleeding occurred, which led the operator to desist. When seen in consultation the patient was considerably shocked. She was transferred to the hospital, the abdomen opened, and a dead child extracted; the uterus was amputated, the fundus, tubes, and ovaries were removed, and the stump was fixed in the lower angle of the wound. On examination, a tear in the posterior wall of the vagina, sufficiently large to admit four fingers, was found communicating with the abdominal cavity. This wound was closed by suture from above, and the abdomen closed without drainage. The patient made a satisfactory recovery.]

Experimental Study in Hemorrhage, and its Bearing on the Treatment of Ruptured Pregnancy.—Robb (*Amer. Jour. Obstet.*, October, 1908) contributes a paper giving the results of thirty-one experiments upon animals, in severing the uterine and ovarian arteries for the purpose of studying intra-abdominal hemorrhage. The results indicate that intra-abdominal hemorrhage, such as occurs in women suffering from collapse after the rupture of an ectopic gestation, is not sufficient in itself to cause a fatal termination. Death results from shock often increased by interference. While it may be urged that the lower animals can bear hemorrhage better than the human subject, the extensive severing of vessels more than counterbalanced the difference. By these experiments it was found that clotting probably occurs from within fifteen to twenty minutes after the vessels have been opened, and this time can be known by observing the hemoglobin index. Subcutaneous injection of salt solution probably does not cause renewed hemorrhage. Manipulation of the tissues, disturbing the clot, does result in continuing the hemorrhage. By bandaging the abdomen, or by applying a moderate weight over the lower abdomen, the pulse is made slower and of better quality, and the percentage of hemoglobin is kept up.

Modern Cesarean Section.—Warren and Polak (*Amer. Jour. Obstet.*, October, 1908) contribute papers upon this subject. Warren describes 5 cases of successful section and one case of a young primipara, weighing 200 pounds, who had a true conjugate of three and one-fourth inches. Spontaneous labor and forceps failed. The head was exceedingly hard, and the conditions such that other operations were rejected and the patient delivered by section. She died of sepsis on the third day. This case illustrates the danger of attempting delivery by other methods before

resorting to section. As usually happens, interference by forceps was practised by the attending physician before summoning consultation. Warren draws attention to the frequent occurrence of overgrowth of the fœtus and the resulting dystocia. He is in favor of the elective section.

Polak's record of 14 cases gives the recovery of the mother in 13, and 1 death. In some of the cases the patient was sterilized by the removal of the Fallopian tubes. In several, complications of varying degree arose, especially in those in whom labor had been going on some time before operation. Nine of the operations were performed for contraction of the pelvis; 3 were for dystocia resulting from ventrofixation of the uterus. Two patients were operated upon for tumors, which became lodged in the pelvis, preventing the descent of the child. The abdominal incision was made one inch to the right of the median line, taking the umbilicus as its central point. The uterus was incised within the abdominal cavity. In one case a tourniquet was used to control hemorrhage. The uterus was closed by chromicized catgut, the stitches including the peritoneum and muscle, but not passing through the endometrium. Three pregnancies have occurred in patients operated upon. The uterus has developed normally in these cases and spontaneous delivery occurred after induced labor. In 2 cases a gauze drain was used, and it was necessary to tampon the uterus to prevent hemorrhage. Chloroform and oxygen proved a very acceptable anesthetic. It was noticeable that the fœtus was not anesthetized. Ergotole was given, two injections of 30 minims, just before the anesthesia was started and after the delivery of the child. In the fatal case the patient had an intestinal fistula at the site of one of the abdominal sutures, caused by a needle puncture, and inclusion of the gut in the suture at the time of operation. A mixed infection followed which attacked the respiratory tract, the patient dying of pneumonia.

GYNECOLOGY.

UNDER THE CHARGE OF

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The Results of the Radical Vaginal Extirpation of the Uterus for Carcinoma of the Cervix.—C. STANDE (*Zent. f. Gynäkol.*, 1908, xxxii, 1201) makes a longitudinal incision through each lateral wall of the vagina, extending the incision deep into the parametrium. This enables him to remove a large portion of the pericervical tissue to which he attaches greater importance than to the removal of glands. He has operated in this way upon 104 patients, 21 of whom died as the immediate result of operation. The greatest danger in this method lies in infection through the vaginal incision, which was the cause of 9 deaths. Injuries to the bladder occurred six times and to the uterus six times. Recurrences of the carcinoma have appeared in 39 cases, the recurrence being located usually in the scar. In only three instances has the recurrence been in

the glands, one of which was in the inguinal glands. In 31 out of the 39 cases the recurrences were manifested during the first year, 5 during the second, 2 during the third, and 1 during the fourth. In 8 of the cases operated upon it was not possible to remove all of the growth, and 4 of these died as the immediate result of the operation, and 4 from recurrences. In addition to the 104 cases operated upon, Stande has had 52 cases of carcinoma of the cervix, 13 of which refused operation; the others were considered inoperable. Recurrences have not appeared on 17 out of 41 cases, or 41.5 per cent. under observation for five years or more since operation.

A New Method of Extirpating both Appendages.—O. BEUTTNER (*Zent. f. Gynäkol.*, 1908, xxxii, 1033) makes two transverse incisions in the fundus extending into the uterine cavity and including between them a wedge-shaped piece of the uterus with the insertion of both tubes and the attachment of one or both ovarian ligaments at the sides. This wedge-shaped piece is then divided in the median line and each appendage is liberated from the uterus outward, an ovary being left if possible. In this respect the method has the same advantages as that of Faure, in which the uterus is divided in the median line to the internal os and each half of the cervix amputated, the halves of the uterus and the appendages being then freed from within outward. In women still menstruating Beuttner, however, desires to retain the uterus and he finds, moreover, like Dührssen that this method of resecting the fundus has a very favorable effect in curing a chronic metritis.

A New Intraperitoneal Method of Shortening the Round Ligaments.—W. LATZKO (*Zent. f. Gynäkol.*, 1908, xxxii, 1278) describes a method of shortening the round ligaments which he has employed in over 100 cases during a period of eight years, with no accidents and only exceptionally a recurrence of the retroversion. The round ligaments at points as remote from the uterus as possible are sutured to the fundus in the median line, and beginning at this point the loops of the round ligaments thus formed are sutured together by through-and-through sutures and to the uterus in the median line anteriorly. The loops are thus brought together as far toward the cervix as possible, below which point the two newly made folds of the broad ligaments are also sutured to the anterior wall of the uterus in order to prevent the entrance of a loop of intestine into the pocket otherwise formed.

Perforating Wounds of the Uterus Inflicted during the Course of Intrauterine Instrumentation.—HEINECK (*Surg., Gyn., and Obst.*, 1908, vii, 424) believes pseudoperforation of the uterus though of exceptional occurrence, is a clinical condition and that spontaneous perforations of that organ, due to preëxisting pathological conditions of it, can and do occur. Heineck insists that perforating wounds of the uterus, whether intraperitoneal or extraperitoneal have a morbidity and a mortality—conditions which increase in direct ratio with the inexperience, the carelessness, the surgical ignorance, and the surgical uncleanliness of the operating surgeon. In the 154 tabulated cases 42 had a fatal ending. Of the 66 cases, in which expectant treatment was employed, 21 resulted fatally. Laparotomy, including apparently necessary intra-abdominal work, was

performed seventy-two times. In this class 17 deaths are recorded and 3 unstated results. Vaginal hysterectomy was done fifteen times, resulting four times in death, and in one no result is given. Heineck expressly states that dilatation of the cervical canal and instrumental curettage of the uterine cavity are, owing to their associate dangers, not office operations. In these operations general anesthesia is advised and the following rules suggested: (1) Ample cervical dilatation during which the cervix should be steadied should be a preliminary step to uterine curettage. (2) Intra-uterine instrumental maneuvers should be attempted only by those (*a*) who are thoroughly conversant with modern surgical asepsis and antisepsis; (*b*) who are capable of recognizing malpositions of the uterus and pathological conditions of that and of neighboring organs; and (*c*) who are acquainted with the treatment of the dangers incident to the successive steps of the intra-uterine operation they are performing. Heineck advises once the uterus is perforated, suspension of all further intra-uterine instrumentation except careful removal of the uterine contents by a finger or, while the uterus is being watched through a laparotomy incision, with a curette. In 2 cases swabbed with carbolic acid death followed. Intra-uterine irrigation following such perforations are opposed. Vaginal hysterectomy is opposed. The conditions in uterine perforations indicating laparotomy are the presence of infection, large-sized or multiple perforations, the presence of coexisting vascular, omental, or intestinal lesions, and prolapse of viscera through the opening.

Primary Implantation of an Ovum in the Pelvic Peritoneum.—Hirst and Knipe (*Surg., Gyn., and Obst.*, 1908, vii, 456) state that in order to substantiate the claim that there has been a primary implantation of an ovum in the peritoneum, the presence of the following conditions is necessary: (1) A normal condition of the tubes, ovaries, and broad ligaments, except where the ovum is implanted; (2) no penetrations of the intraligamentary space from the ovarian fimbria; (3) no intraligamentary rupture of the tube; (4) no escape of the ovum from the uterine cavity; (5) proof that the peritoneum constitutes the reflexa of the ovum. Galabin and Witthauer have each reported an authentic case of primary implantation of the ovum in the peritoneum, and Hirst and Knipe report a third that meets the requirements just mentioned. In passing, mention may be made of the inaccuracy of the first condition, as pathological conditions of the tubes, ovaries, or broad ligaments may coexist and even antedate such implantation.

The case of Hirst and Knipe is as follows: The patient, aged thirty-one years, had one child seven months ago after a normal labor and has had no other pregnancy. Her menses began at the age of fourteen years and have always been regular and normal; her family history was negative. Three months after the birth of her child, which she is nursing, menstruation recurred twice a month. During all the six days just preceding her admission to the hospital she flowed. On the sixth day while stooping over she was seized with pain in the lower part of the abdomen, very severe in character and producing faintness. Pain and syncope recurred six times during the evening. Operation was one March 27, 1907. Free blood in moderate quantity was found in Douglas' pouch. On the posterior surface of the left broad ligament

was a spherical tumor, with a small orifice on its surface from which blood was exuding. The tubes, ovaries, uterus, and remainder of the broad ligaments were perfectly normal. The tumor was covered with peritoneum. A small embryo was found in it. A microscopic examination demonstrated the capsule to consist of an outer and an inner layer of fibrous connective tissue between which an extensive extravasation of blood had occurred. Around two-thirds of the periphery of the ovum may be distinguished nuclei of the endothelial cells of the peritoneum. At the point of erosion chorionic villi are seen protruding into the orifice.

Physical and Psychical Conditions Persisting after Mutilating Operations on the Female Generative Organs.—HOLCOMBE (*An. Gyn. and Ped.*, 1908, xxi, 361) believes physical and psychic conditions frequently persist for long periods of time after mutilating operations on the female pelvic organs, but that they are commonly in evidence before the operations. The opinion is offered, however, that not infrequently such conditions result from operation. In this latter class Holcombe believes that either the mental and general physical conditions are not well known, or the operation is not a proper one, although it is admitted that the gynecological surgeon may have such knowledge and yet believe the surgical treatment is imperative. Holcomb emphasizes the necessity for careful after-treatment of patients subjected to operations on the female genitals.

OPHTHALMOLOGY.

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The Operative Treatment of Optic Neuritis.—VICTOR HORSLEY (*Ophthalmoscope*, September, 1908, 658) sums up his position as follows: Optic neuritis should be treated as soon as detected; operative treatment should consist, in the absence of other indications, in opening the subdural space in the temporal or subtentorial region. The bore-hole and release of fluid ought to be unattended by any risk if the aseptic technique is adequate. Against the opinion that the neuritis is no help in the localization of the tumor, Horsley asserts that the lesion is upon the side upon which the neuritis is the more marked, or is the older. While nothing can be done for cases which exhibit well-marked atrophy, there are all sorts and degrees of atrophic changes which may be present and which ultimately disappear, with good results as regards vision, if the source of the neuritis be removed.

The Treatment of Congenital Cataract.—COLLINS (*Ophthalmoscope*, September, 1908, 675) advises to wait before needling, with which operation it is best to begin in nearly all cases, until the child is ten months old so that the eye may be sufficiently developed, the aqueous present in adequate amount, etc. Iridectomy should be performed if the pupil does not dilate well under the mydriatic. In Morgagnian cataract it is advisable to evacuate the chamber to obviate increased tension. If a dense membrane remains it should be displaced downward and backward.

Punctate Atrophy and Pigmentation of the Choroid.—GEPP (*Archiv f. Augenh.*, 1908, lix, 383) reports a very unusual instance of punctate atrophy of the choroid in a young man without specific history. The earliest appearances were noted in the extreme periphery and consisted of light-colored spots; these increased in size and were gradually surrounded by a pigment border, new foci at the same time extending toward the centre and gradually undergoing the same changes. There was a central scotoma for form and color, but the fields were not contracted.

Treatment of Fistula of the Lacrymal Sac by Electrolysis.—LOTIN (*Westnick. Opht.*, 1907, 655) passes a current of 5 ma. during five minutes between the anode, which consists of a silver or platinum wire inserted into the fistula, and the cathode placed in the nares of the same side. The current is reversed at intervals. Rapidity and efficacy are claimed for the method to a remarkable degree even in invertebrate cases. In stenoses an isolated sound like the one recommended by Lagrange is employed, connected by preference with the cathode.

Dangers of Radium in Paste.—LE BON (*La clin. ophtal.*, 1908, No. 18, 293), to obtain the maximum of radiations from radium, has found that a paste applied directly to the desired region is the most effective. Accordingly, in therapeutics a paste has been applied immediately upon the skin, or cavities, in the treatment of nevus, angioma, epithelioma, eczema, etc. In a nevus of the forehead and eyelid of a restless infant so treated, DE COURMELLES observed that the paste after drying was exfoliated with the underlying tissue in scales; if the same event had occurred in an organ or cavity, extensive burns would have resulted. The reporter proposes to return to the use of tubes; although the latter are somewhat more troublesome, they are readily antisepticized and do not entail the above risks.

Extraction of Cataract in a Rhinoceros.—MATER (*Woch. f. Ther. u. Hyg. d. Aug.*, i, 42), with the aid of fourteen assistants, six journalists, three photographers, and ten attendants, extracted a cataract from the eye of a rhinoceros in the New York Zoological Garden. The operation lasted about half an hour and gave a successful result, which is by no means always the case in the lower animals. The operation was done under anesthesia for which purpose 900 grams of chloroform and 200 grams of ether were required, several of the attendants being nearly overcome during the process. A great difficulty was keeping watch upon the heart of the animal for the skin was so thick that the pulse could not be perceived.

Ophthalmia from Exposure to Snow.—GONIN (*Annal. d'oculist.*, September, 1908, 161) observes that references to disturbances of vision from exposure to the bright light reflected from snow occurs as early as in Xenophon's *Anabasis*, who states that he was compelled to abandon some of his soldiers on the route whose eyes had been "overwhelmed" by the snow. Modern writers have shown a disposition to question its occurrence. Such skepticism is doubtless due to the improper designation "snow-blindness" which the affection has popularly received. As a matter of fact the lesion most commonly observed is really a mild form of conjunctivitis, due in all probability to the ultraviolet rays, as is the case also in inflammation from exposure to electric lights. The retina is protected by the well-known property of the crystalline lens to absorb those rays and thus prevent their injurious effect upon the deeper structures. Hemeralopia, nyctalopia, and erythropsia have all been occasionally observed, but the mechanism of their production is obscure.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Interdependence of the Glands with Internal Secretions.—In a long and elaborated series of experiments, EPPINGER, FALTA, and REUDIGER (*Ztschr f. klin. Med.*, 1908, lxvi), show that the physiological actions of the thyroid gland, the adrenals, and the pancreas are intimately connected. The extirpation of one of these glands acts upon the organism in two ways, directly through the loss of internal secretions, and indirectly by a disturbance in the function of the glands. The simple direct effect of extirpation of the thyroid gland upon the general metabolic process, showed itself, in starving dogs, particularly by a diminished excretion of nitrogen. The simple direct effect of an oversecretion of the adrenals, imitated by injections of adrenalin in starving dogs, was seen in an increased excretion of nitrogen and in the appearance of glycosuria. It was found now that extirpation of the thyroid had an indirect influence upon adrenalin glycosuria, for adrenalin glycosuria could not be produced in thyroidectomized dogs. By feeding these dogs thyroid extract, however, they could again be made susceptible to adrenalin glycosuria. No less remarkable was the effect of injections of adrenalin in dogs whose pancreas had been removed. Following injections of adrenalin in such dogs, the excretion of sugar and output of nitrogen was much increased above that observed in dogs

whose pancreas had been removed and in whom adrenalin had not been injected, and the dextrose-nitrogen co-efficient was almost doubled. The removal of the thyroid secretion from the body by extirpation of the gland had, on the other hand, an exactly opposite effect on dogs whose pancreas had been removed. Preliminary removal of the thyroid decreased the excretion of the nitrogen and sugar when the pancreas was removed. If the two glands were removed simultaneously the decrease in nitrogen and sugar output was not observed until a day or two after the operation.

The experiments show that, under normal circumstances, the thyroid exerts an inhibitory action upon the internal secretion of the pancreas. When the thyroid is removed, the inhibitory influence upon the function of the pancreas is done away with and there is a "hyperpancreatism," while excessive secretion of the thyroid gives rise to a partial insufficiency of the pancreas and to an increased action of the adrenal. The adrenals also possess a marked inhibitory action, even greater than the thyroid, upon the pancreas, and besides seem to increase the action of the thyroid. The secretion of the pancreas inhibits both the action of the adrenals and thyroid. Further experiments seemed to show that the sympathetic nervous system and vagus nerves were at least in part responsible for the conduction of these influences from one gland to the other. It could be shown that the glycosuria produced by puncture of the floor of the fourth ventricle, was analogous to adrenalin glycosuria, inasmuch as removal of the thyroid gland prevented the appearance of glycosuria following injury to this particular portion of the nervous system. The adrenal glands are known to bear a close relationship to the sympathetic nervous system, and it seems quite probable that increased action of the chromaffin system in general leads to an overexcitability of the sympathetic nerves, while loss of function results in decreased excitability. Not only the adrenals, but the thyroid as well, may act as a direct excitant to the sympathetic nerves, for adrenalin mydriasis could be obtained constantly in normal and even thyroidectomized dogs by the feeding of thyroid extract. The thyroid seems, however, to have a double action and influences the vagus nerve as well as the sympathetic nerves.

Between the pancreas and the nervous system it is much more difficult to establish a relationship, though it seems very likely that the pancreas is not only influenced by, but influences, the vagus nerves. To show that the internal secretion of the pancreas is under the direct control of the vagus nerve, a number of experiments were performed. It was found that when the vagus was paralyzed by the administration of pilocarpin, excessive internal secretion of the pancreas, or "hyperpancreatism," resulted, and injections of adrenalin failed to produce glycosuria. On the other hand, injections of atropine seemed to stimulate the vagus, and so depress the function of the pancreas that the effect of thyroidectomy was outbalanced, and the injection of adrenalin in thyroidectomized dogs to which atropine was administered, gave rise to glycosuria.

The application of the results of these experiments to the phenomena observed in certain diseases of the ductless glands is obvious. Among other conclusions the authors draw attention to the close relationship between changes in function of the chromaffin system and diabetes

mellitus. It is possible that diabetes may be brought about through some perversion of the function of the chromaffin system as well as by actual disease of the pancreas itself.

In connection with this work some recent experiments of PEMBERTON and SWEET (*Archiv. Int. Med.*, 1908, i, 628) are of great interest. They have studied in dogs the effect of injections of the extracts of various organs upon the flow of pancreatic juice after the administration of secretin. By means of a calibrated cannula, inserted in the pancreatic duct, they were enabled to measure with accuracy the rate of flow of the pancreatic juice. They have found that extracts of the adrenal glands and of the nervous portion of the pituitary body contain a substance which cuts short the flow of pancreatic juice excited by secretin, and prevents the stimulation of the pancreas by secretin when its injection precedes the secretin. Both extracts produce a rise of blood pressure, but the inhibitory action is not due to this factor, for in isolated experiments a rise of blood pressure was obtained without an inhibition of the flow of pancreatic juice. Section of the vagi had no influence upon the action of the adrenal and pituitary extracts. As far as could be learned, this inhibitory action upon the secretion of the pancreas was specific for the adrenal and pituitary bodies. Injections of extracts of the brain, of the liver, and of the testes, of atropine, and of digitalis had no effect upon the flow of pancreatic juice. It is interesting to note, in the light of the experiments of Eppinger, Falta, and Reudiger, that extracts of thyroid gland were equally ineffective.

The Connection Between the Proteolytic Ferments of the Leukocytes and General Immunity.—JOCHMANN (*Ztschr. f. Hyg. und Infectkrank.*, 1908, lxi, 71) has made some experiments to determine whether the proteolytic ferments contained in the polymorphonuclear leukocytes are in any way related to bactericidal substances or to the "microcytase bactericidal alexin" of Metchnikoff, which, according to him, is supposed to reside in the polymorphonuclear leukocytes. Jochmann could not not find that the enzymes of the leukocytes had any destructive action upon living bacteria, nor were they capable of hemolyzing living red blood corpuscles. The enzymes do not act as a complement, nor do they destroy toxins. The enzymes do, however, digest dead bacteria in vitro, and Jochmann thinks that this property explains the disappearance of bacteria ingested by polymorphonuclear leukocytes.

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